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DEHYDRATION: AN ANALYSIS OF THE METHODS USED IN DIAGNOSIS

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DEHYDRATION is a commonly encountered condition. It may be caused by inadequate water intake, vomiting, diarrhea, fistulas from the gastrointestinal tract, prolonged suction by Wangensteen or Miller-Abbott tubes, intestinal obstruction, prolonged sweating, draining wounds, excess metabolism, abnormal kidney excretion, diabetic acidosis, and extensive burns.

Early recognition and treatment of this disorder is obviously of the utmost importance, and various clinical and laboratory methods have been utilized to this end. It is our purpose in this paper to evaluate these methods from a study of the literature and from personal observation.

Certain fundamental concepts should first be stated. Water comprises about 70 per cent of the body weight, and approximately three-fourths of this is intracellular water, which is rich in potassium and contains practically no sodium or chlorides. The remainder is extracellular water, which is rich in sodium and chlorides, and poor in potassium. The extracellular water is divided between the blood plasma and the interstitial fluid.

If the body is deprived of water, both intracellular and extracellular water is lost, and there is a parallel loss of body water and salts (2). This is characterized by thirst, oliguria, and azotemia, but only slight changes occur in the concentration of the blood. Our own experimental data (unpublished) indicated that dogs subjected to water deprivation showed remarkable constancy of the hematocrit, plasma protein, and serum sodium values for several days, when slight elevations took place. Decreased urinary output, marked thirst, and weight loss were early findings, however.

If, on the other hand, the body is subjected to abnormal salt loss, such as in severe vomiting or diarrhea, the sodium deficiency leads to a reduced extracellular fluid volume, with rapid development of hemoconcentration and the absence of thirst. As will be brought out later, the proper recognition of these types of dehydration is of paramount importance in therapy. The common occurrence of mixed dehydration probably explains the failure of many workers to distinguish the two types, as pointed out by Nadal, Pedersen, and Maddock (25).

Dehydration, if severe, may lead to circulatory failure, the so-called "electrolyte shock." Loss of plasma volume is compensated for partly by absorption of fluid from the tissues and vasoconstriction, but when this mechanism fails, the blood pressure drops, anoxia develops, and the shock syndrome manifests itself (23). At autopsy, petechial hemorrhages in the liver, spleen, pleura, meninges, lungs, heart, brain, and adrenal glands are found, together with serous effusions, capillarovenous congestion, and parenchymal necroses. These changes result from alterations in the capillary permeability, because of hemoconcentration and subsequent anoxemia (12).

The methods used in the diagnosis of dehydration will be discussed separately under the following headings: (1) clinical symptoms and signs; (2) measurement of the urinary output; (3) determination of the blood specific gravity, and serum and plasma protein concentration; (4) red-cell count, hemoglobin, and hematocrit determinations; (5) study of the electrolyte pattern of the blood plasma; (6) blood volume and available fluid-volume determinations; and (7) estimation of the fluid need of the interstitial tissues.

Clinical symptoms and signs. Slight degrees of dehydration are difficult to recognize, dryness of the buccal and oral mucosa being the best index. However, it is estimated that a loss of 6 per cent

or more of body weight in water is accompanied by characteristic clinical findings: warm, dry, wrinkled, inelastic skin; soft eyeballs; dry tongue and thick speech; dulled sensorium; rapid pulse; and acidosis (30).

Most of the signs and symptoms are produced by a deficit of extracellular electrolyte, and may progress to the typical picture of circulatory collapse (electrolyte shock). Thirst is not an obligatory accompaniment of dehydration, and is dependent solely on water loss (11). Loss of weight takes place rapidly, and anorexia, nausea, muscle cramps, and actual tetany are frequent findings (29).

Measurement of the urinary output. A total urinary output of 1,500 cc. in twenty-four hours is generally considered satisfactory. Water deprivation usually produces some degree of oliguria. However, it must be stressed that the degree of oliguria is not an accurate index of the extent of dehydration, as a certain minimum urinary volume is inevitable as long as the blood pressure is high enough to insure glomerular filtration. It takes profound shock and hypotension to produce anuria (25).

Furthermore, dehydration causes a diminished renal blood flow, and thus impairs the concentrating power of the kidneys, and allows the urinary volume and specific gravity to be normal (22).

Determination of the blood specific gravity, and serum and plasma protein concentration. The normal specific gravity of whole blood is 1.0566 for males and 1.0533 for females. Normal plasma proteins range from 6 to 8 gm. per cent (28). These determinations can be made simply and rapidly at the bedside by the "falling drop" method of Kagan (20), an extension of the work of Barbour and Hamilton (5). This method has been compared with the determination of specific gravity by weight, by total solid content of plasma, and by plasma protein on refractometric analysis, and found most accurate (31).

The specific gravity of blood and plasma is increased in dehydration and shock, and decreased in hemorrhage and edema (13, 14). Many dehydrated patients have hemoconcentration, as shown by increased blood specific gravity and elevated serum proteins. The determination by means of the specific gravity of peripheral blood is considered 25 times as sensitive as that by means of the red cell count or hemoglobin in the measure of dehydration (28).

Dehydration is probably the most common cause of hyperproteinemia (19). Hemoconcentration may be recognized by elevated serum protein concentration, even in the presence of a normal serum electrolyte pattern (22). It must be remembered that hyperproteinemia may also be produced by a variety of infectious diseases, such as carcinoma, and cirrhosis, although these usually cause a reversal of the albumin-globulin ratio as well (27).

Considerable interstitial fluid may be lost before any marked change becomes apparent in the concentration of serum or plasma protein. This constancy has been shown by concentration and dilution experiments on dogs and human beings (24). Severe chronic dehydration may even cause hypoproteinemia, because of destruction of the blood proteins. Similarly, hypoproteinemia before hemoconcentration may cause plasma protein not to rise above normal levels (26).

With such pitfalls in mind, most observers, nevertheless, conclude that these determinations are efficacious indicators of hemoconcentration and related blood volume changes (3). Rise in serum proteins served as a reliable index of dehydration in dogs subjected to pyloric ligation (15) and high intestinal obstruction (4), and in infants suffering from diarrheal disease (17).

Red cell count, hemoglobin, and hematocrit determinations. Hematocrit determinations can readily be made by the method of Wintrobe (32). Normal cell volume ranges from 42 to 50 per cent in males, and from 39 to 43 per cent in females. An increase in the hematocrit reading generally indicates water loss, and a decrease, blood loss.

The red cell count, hematocrit, and hemoglobin, as well as the specific gravity of the blood and plasma proteins, are physical measures of hemoconcentration, and as such are increased in dehydration. The relationship of these factors to each other is a constant one.

These tests may be normal in slight dehydration because of the efficiency of homeostatic mechanisms in maintaining constancy in the blood by drawing on interstitial fluids. Furthermore, they may be misleading in the presence of anemia or polycythemia. However, in the salt-loss type of dehydration, hemoconcentration is rapid and progressive, and is observed early.

Study of the electrolyte pattern of the blood plasma. The principal base of blood and extracellular fluid is sodium, while potassium is the chief base of intracellular water. If sodium is depleted, water must be lost to keep the concentration of substances in solution at the same normal level. The chloride ions can be replaced by bicarbonate ions, but sodium is not replaceable, and consequently has the greatest role in maintaining extracellular fluid volume (9).

Gamble (15) has shown in classic experiments, by producing pyloric obstruction in dogs, that loss of the sodium ion is the significant factor in dehydration. These dogs could not be restored to normal with glucose solution, water, or water plus the chlorine ion, but were restored with sodium chloride solution.

This base depletion may be a primary cause of dehydration (e.g., biliary, pancreatic, or intestinal fistulas), or a secondary effect of prolonged dehydration that has caused impaired renal function (30).

Water balance cannot always be estimated accurately from balances of sodium or potassium, as dehydration of about 2 per cent of body weight can occur without corresponding changes in the salt or solid content (25). The serum electrolytes tend to maintain a normal pattern, and by the time the serum salt finally falls, the clinical signs and symptoms of dehydration are already in evidence. This constancy is dependent on normal renal function, as shown in experimental administration of mercurial diuretics to rabbits (21).

Other chemical changes of less significance take place in dehydration. Dogs with high intestinal obstruction showed decreased total base and chlorides, and increased carbonates, protein anions, sulfates, and phosphates (4). Other similar experiments showed a rise in plasma carbon-dioxide combining power, nonprotein nitrogen, and urea nitrogen (17).

An interesting controversy exists as to the cause of death in high intestinal obstructions and fistulas, previously thought to be due to dehydration and loss of sodium and chlorides. Scudder and coworkers (29, 8) have demonstrated experimentally, in cats, a great rise in blood potassium, which they believe is a toxic factor responsible for death. Other workers (6) have failed to discover any evidence that potassium contributes to the symptoms or death of animals with high intestinal obstructions and fistulas.

Clinically, the determination of the blood sodium is impractical because it is too time-consuming. It is suggested to rely on the blood chlorides, and, as a substitute for sodium, to measure the carbon-dioxide combining power. This shows the amount of sodium ions in excess of chlorine ions (9).

Blood volume and available fluid-volume determinations. Anhydremia produces hemoconcentration, which eventually produces a decreased blood volume, although tissue water is used up first (2).

The plasma volume is a function of the total volume of "available fluid," and is subject to large individual variations with weight, surface area, age, and sex. Blood-volume determinations are usually made with T-1824 or Evans' blue dye, and available fluid determinations are made by the sodium-thiocyanate method (16).

Although some observers (10) believe that available fluid volumes can be used to estimate dehydration or superhydration, it is the opinion of most men that these tests are not applicable to the study and treatment of early clinical dehydration. The tests are difficult, time-consuming, and subject to great variation.

Estimation of the fluid need of the interstitial tissues. This determination is made by making an intradermal wheal of normal salt solution, and is known as the McClure-Aldrich test. The test is inversely proportional to the tissue avidity for water. Hopps and Christopher (18) used it in postoperative patients and found it a sensitive and reliable index to the state of hydration and a useful guide to optimal fluid administration, provided that the electrolytic balance was considered. The same conclusions were arrived at by Appel and Brill (1), although they noted that the disappearance time of the wheal was also decreased in edematous conditions, toxemias, and diseases of the peripheral arteries.

On the other hand, Nadal found that in subjects deprived of water and dehydrated 6 per cent of their body weight, the McClure-Aldrich test was unreliable (26). Simeone (30) believes the test to be of questionable value.

Obviously, further work must be done with this test before any definite conclusions can be drawn as to its value in the diagnosis of dehydration.

Replacement therapy. A detailed discussion of replacement therapy is beyond the scope of this paper, yet a few suggestions as to its management in relation to the diagnostic methods discussed are in order.

Scudder (13) and others (4) are in favor of rationally directing the treatment by watching the concentration of the blood, as evidenced by determinations of the specific gravity of the blood and plasma, and calculation of the plasma proteins, and hematocrit. These tests will determine the degrees of water loss and water-plus-protein loss, anticipate the onset of shock, detect dehydration in the presence of anemia, and predict the approach of the edema level of proteins.

Simeone (30) advocates watching the nature of the shift in the electrolyte pattern as a guide for replacement therapy.

Coller and Maddock (9) believe in the replacement of fluid on a volume-for-volume plan. In

essence, their method consists of giving water or glucose solution for simple dehydration, and saline or Ringer's solution for extracellular dehydration.

The former is to compensate the loss of water of vaporization and to insure a satisfactory daily urinary output; the latter replaces, volume by volume, abnormal gastrointestinal fluid losses.

SUMMARY AND CONCLUSIONS

1. Dehydration is a commonly encountered condition and has a multitude of causes.

2. The early recognition and treatment of this disorder are of the utmost importance.

3. The essential differences between extracellular and intracellular dehydration are disdiscussed.

4. The pathogenesis and pathology of dehydration are described.

5. The methods used in the diagnosis of dehydration are discussed and evaluated.

a. Clinical symptoms and signs are characteristic, but appear late.

b. Measurement of the urinary output is not an accurate index of the extent of dehydration.

c. Hemoconcentration is an early and reliable finding, as evidenced by an increase in the red-cell count, hemoglobin, hematocrit, blood specific gravity, and serum and plasma protein concentrations. Certain pitfalls must be borne in mind in evaluating these tests.

d. Study of the electrolyte pattern of the blood plasma is helpful but time-consuming, and changes are slow to appear.

e. Blood-volume and available fluid-volume determinations are generally not applicable to the study and treatment of early clinical dehydration.

f. The McClure-Aldrich test as a means of estimation of the fluid need of the interstitial tissues requires further study.

6. The various methods used in the diagnosis of dehydration are of great value in the rational direction of its treatment.

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HEPARIN AND DICUMAROL

Collective Review

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THE purpose of this work is to make a survey of the record of investigational and clinical experiences of the various groups who have been and are still working with heparin and dicumarol, and to report our clinical experiences to the evergrowing collection of cases that are appearing in the literature constantly since renewed interest in heparin was stimulated by the work of Murray and his coworkers in Canada (30, 31, 32, 33), Crawford and Jorpes in Sweden (9), and many other groups throughout this country and other countries. Furthermore, the stimulation of interest in the synthetic hemorrhagic agent dicumarol was brought about by the much quoted brilliant work of the chemists, Karl Paul Link and his associates (8, 17, 41a).

In the discussion of this work we will present the opinions of the enthusiasts, who are numerous, as well as the opinions of the conservatists, who are very few. The consensus is that the work on these two hemorrhagic agents will rank in importance to the medical profession along with such discoveries as of vitamin K, adrenaline, and of many other physiological agents that have been isolated and later applied to clinical use.

It is hoped by many that eventually, when all the kinks have been straightened out, we can remove the fear of the horrible experiences associated with the sudden deaths from vascular accidents caused by thrombosis and embolism, and prevent pain and suffering caused by postoperative thrombophlebitis. It is borne out by many surgical records that mortality rates are increased by vascular accidents.

Before consideration of the work that has been done with heparin and dicumarol, it is well to review briefly the history of the discovery and development of the use of these hemorrhagic agents, and also to review briefly the physiology of blood coagulation. We will discuss these particulars individually and collectively and according to the nature of the work that has been accomplished.

Heparin products used were furnished by Connaught Laboratories, Lederle Laboratories, Hoffman LaRoche, and Upjohn Company. Dicumarol was furnished by Abbott Laboratories.

An excellent review of the history, chemistry, physiology, and clinical application of heparin appeared in March, 1939, by Morton F. Mason (26). An abstract of this review and other reports on these particulars of the subject tell us that the first recorded observations of the anticoagulant properties of heparin were made in 1916 by J. MacLean, a medical student at Johns Hopkins University, while working in Howell's laboratory and studying the thromboplastic behavior of several phosphatides. Two were found to inhibit clotting: cuorin, prepared from heart muscle by the method of Erlandsen, and the heparphosphatide of Baskoff, isolated from dog liver. Shortly afterward Howell and Holt made an extensive study of heparphosphatide. They observed that although the cuorin prepared by MacLean was identical with that of Erlandsen, the heparphosphatide he had isolated differed somewhat in its properties and nitrogen-phosphorus ratio from the original preparation of Baskoff. For the heparphosphatide with which they were dealing, Howell and Holt proposed the name "heparin" to indicate its origin in liver, and they described in detail the procedure they used in its preparation to free it from cephalin.

In a collective review of this subject of heparin, A. J. D'Alessandro (10) states that Howell concentrated on the purification of this physiological anticoagulant and contributed practically all of our knowledge of heparin until 1929 when Best of Toronto became interested in it. Best persuaded Charles and Scott of the Connaught Laboratories in Toronto to undertake further purification of heparin than had previously been possible. Charles and Scott succeeded in obtaining a crystal barium salt from ox lung in 1933. They found that the barium can be completely removed from this solution and that the heparin can be stored as a dry powder, from which a solution can be made and sterilized by filtration. Charles and Scott also contributed confirmation of the fact that heparin is widely distributed in the tissues of the body and is especially abundant in the lung. Their product yielded 500 U/mgm. Schmitz and Fischer, working independently in Copenhagen in the same year, had succeeded in obtaining a pure

brucine salt of heparin. Consequently, extensive experimental and clinical trial of this pure heparin was carried out by various investigators, especially Best and Murray in Toronto (30) and Jorpes, Holmgren, and Wilander in Sweden (18). We have used it occasionally since 1939 as various indications have arisen in our work in The Pfeiffer Surgical Clinic.

During the past two years since D'Alessandro's collective review (10) was written, results from the clinical experiences of many workers (1, 1a, 2, 6, 14, 43) have accumulated and established more definitely the value of heparin in many clinical conditions. Also, the clinical experiences with dicumarol are establishing this agent as a drug of more and more importance, and it may eventually take the place of heparin. The relative value of these two drugs as to their advantages and disadvantages will be discussed later in this work. Some of the outstanding work along these lines that has been recently reported is the interesting work of J. A. Evans (14) of the Lahey Clinic, on the combined use of heparin and dicumarol. Two groups at the Mayo Clinic, Bollman and Preston (6), and Allen, Barker, and Waugh (1, 1a), have reported some very significant investigational and clinical results from the use of these hemorrhagic agents. These reports also will be discussed later. The work of Bauer at the Mariestad Hospital in Stockholm gives more evidence of the value of these hemorrhagic agents in clinical use. An ever-increasing interest in them is manifested by many other reports of investigation in their various phases.

A brief reference to the physiology of blood coagulation is made in order to lead to a better understanding of the discussion as to the mode of operation of these agents, dicumarol and heparin. W. H. Howell (16) states:

"For a generation or more it has been accepted by most of the workers in this field that the clotting of blood takes place in two steps; first, the formation of thrombin from prothrombin and, second, a reaction between thrombin and fibrinogen which leads to the deposition of fibrin needles and the gelatination of the blood. The factors entering into these reactions are expressed in the schema first used by Morawitz, which is as follows:

Prothrombin plus Ca ions plus thromboplastin
equals thrombin
Thrombin plus fibrinogen equals fibrin.

The schema is incomplete in that it fails to give the nature of the reactions in the two equations. On this point at present there is great diversity of opinion. It would be interesting to discuss the different views that have been proposed, but it would scarcely be profitable since the weight of evidence at present does not incline to one view more than another. The schema is lacking also in another respect, namely, that it fails to take into account the role played by the inhibitory substances of the blood and tissues as possible factors in the coagulation process. They do enter in an important way into the clinical applications that are being made of blood physiology."

It is important to mention briefly some of the factors of coagulation brought out in relatively recent advancement in our knowledge because they have a bearing on the clinical application on these hemorrhagic agents, heparin and dicumarol.

The discovery and the synthesis of vitamin K, which is essential to the formation of prothrombin, have led to the most useful clinical application of this vitamin. This discovery by Dam about 1929 coincided with important work by Quick, H. P. Smith, and others on the effect of jaundice and liver disease on the concentration of prothrombin in the blood. In the work done on heparin and dicumarol it has been pointed out by various workers that vitamin K deficiency and liver disease are important contraindications to the clinical use of these agents.

The relative concentration of prothrombin in the blood is readily determined by simple laboratory methods. A reduction to from 10 to 20 per cent of the normal prothrombin concentration is likely to cause a hemorrhagic state. From the practical point of view we are interested in these facts because it is believed that heparin has an inhibitory effect both on the prothrombin or the first stage of coagulation and on thrombin to prevent the second stage, this action being manifested rather promptly. Dicumarol on the other hand, according to experimental conclusions (37), prolongs the coagulation of blood by prohibiting the formation of prothrombin. This mode of action of these agents is used to explain the immediate effect of heparin and the delayed effect of dicumarol as it is believed that there may be enough prothrombin in the blood to continue the coagulation reaction for a variable period of time. It is at this point we observe a gap in our thorough understanding of the physiology of blood coagulation. Later in this paper we will discuss the different views of the modes of action of these agents and point out that vitamin K has no influence on overcoming the established effect of dicumarol.

In the discussion of heparin and thrombosis, D'Alessandro (10) states:

"One most important phase in physiology of heparin of greatest interest to the surgeon is its role in thrombosis or the prevention thereof. The recent advances in the purification of heparin have restored to prominence the classic work of Bizzozero, who in 1882 first emphasized the role of blood platelets in the formation of thrombus. The role of the platelets has helped to differentiate the white thrombus or platelet agglutination, the red thrombus or clot and the mixed thrombus, although most thrombi are of the mixed variety which suggests the role of platelet agglutination as well as of clotting. The very fact that pure white thrombi may form without any detectable evidence of fibrin further aids in isolating this agglutination phenomenon from the clotting role in thrombus formation."

As Best has described the formation of the usual thrombus:

"One may reasonably assume that platelets accumulate at the focus of injury, usually at the intima of a blood vessel and form masses. Fibrin is subsequently deposited within and around this clump of platelets by virtue of the clotting mechanism initiated by these 'altered' platelets. Other cellular elements of the circulating blood then become enmeshed in this network of fibrin and the thrombus grows accordingly downstream in the direction of blood flow. Once formed, a thrombus acts like a foreign body by stimulating the production of thrombokinase and causes further growth by apposition."

It is well to point out here that the administration of heparin and dicumarol do not affect the thrombus already formed. The effect is to prevent the further growth of the thrombus and thereby prevent further disturbance in the physiology of circulation which is caused by progressive occlusion of the vascular tree by the progressive thrombosis. D'Alessandro (10) further states:

"It is important to bear in mind, however, that the latent period of heparin action on blood coagulation is very short, whereas its latent period of action on platelet agglutination is long, sometimes several hours. This would mean that early in heparin therapy white thrombi may still form while coagulation is inhibited. The inhibition of platelet agglutination by heparin is now being explained as a physicochemical reaction based primarily on the strong electric charge of heparin which in some way modifies the electrical potentials or surface tension of the blood platelet."

The chemistry and other properties of heparin are given according to our present knowledge in the collective review of A. J. D'Alessandro (10), a summary of which we include.

Despite the isolation of pure heparin independently in two laboratories and the subsequent extensive research, its exact chemical formula is still unknown. Some workers even doubt the existence of a specific homogenous chemical compound. Jorpes held this view, while Best and his collaborators were equally insistent on the homogeneity of heparin from the same species, a fact substantiated by the recent work of Charles and Todd. They do, however, admit that heparin does differ in different species and is of varied potency in all of these species. The most potent heparin yet obtained is found in the dog.

The work of some observers has led them to believe that heparin is a complex carbohydrate or mucoitin polysulfuric ester represented by the formula:

$$C_{22}H_{29}O_{12}\begin{cases}(OSO_3H)_5\\(COOH)_2\\(NHCOCH_3)_2\end{cases}$$

A complicated structural formula is suggested for heparin by various chemists, but it is not included here because it is primarily of didactic interest. However, the chemists are not in agreement on a final answer to the formula for heparin. It is agreed that heparin is the strongest known organic acid found in the body.

For a more detailed discussion of the chemistry of heparin reference is made to the monograph by Erik Jorpes (18).

D'Alessandro states:

"The most important single chemical property of heparin is its ability to combine with proteins and especially with protamine as was shown by Fischer and Chargaff and Olson. The latter workers observed that heparin and protamine combine in the constant proportion of 0.3 mgm. of heparin to 1 mgm. of protamine, and that in this combined state the anticoagulant action of heparin disappears."

As is pointed out in D'Alessandro's review, this fact would be of marked clinical value were it not for the high toxicity of protamine.

A highly significant property of heparin, particularly in reference to the maintenance of fluid balance, is its lack of osmotic pressure. It has no osmotic effect on red blood cells. It has been shown that the essential chemical constituents of the blood are not affected by heparin. Neither are the red-cell count, the white-cell count, and the hematocrit determinations affected. All the workers in this field confirm the fact that pure heparin has no effect on temperature, blood pressure, or antigenic properties of the individual.

It is general knowledge that heparin is widely distributed in the human body, especially in the

lung, liver, and intestinal mucosa. "Commercially, heparin is obtained from ox lung, 100 pounds of which yields 1 gm. of heparin. The occurrence of heparin has been associated with the heretofore little understood mast cells of Ehrlich. These cells are found widely distributed in the various connective tissues and are characterized by the predominance of large basophilic granules. In the circulating blood these cells are represented by the basophilic leucocytes. It has been noted by Holmgren, Wilander, Jorpes and others that the granules of these mast cells are identical with heparin. Thus, for the first time a definite physiological action can be attributed to the mast cells which are particularly preponderant along capillary and larger blood vessel walls. This fact may account for the fluid state of capillary blood postmortem—a phenomenon previously explained by the anticoagulant action of increased carbon dioxide tension—and indicates the possibility of ready mobilization of heparin in the blood stream when needed. The reaction to toluidine blue is obtained also from cornea, capsule of the lens, iris, and vitreous body, which indicates the presence of heparin here and offers an explanation for the fact, well known to ophthalmologists, that internal eye hemorrhages generally do not clot" (10).

To summarize the mode of action of heparin it is not necessary to discuss the controversial points among the authorities; it will be sufficient to state the general agreements reached. The majority of workers in this field agree that heparin has an inhibitory action both on the prothrombin or the first stage of coagulation, and on thrombin to prevent the second stage. The presence of a component of the serum-albumin fraction is necessary before it can assert its action. Heparin is the normal physiological agent in the circulating blood that maintains the fluidity of the blood. It is evident that the heparin factor and thrombokinase are antagonistic and within certain limits the concentration and excess of either counteracts the effect of the other. It is on the basis of excess thrombokinase that heparin is indicated clinically.

The exact metabolism or disposition of heparin is not known. It is thought probably that it is changed by an enzyme heparinase. This assumption is borne out by some experimental evidence.

The history of the isolation and synthesis of dicumarol is best given in an abstract of a report by Link and Campbell who summarize six years of chemical research (7).

In 1939 Link and his associates isolated and crystallized the active principle in spoiled sweet clover that has been responsible for hemorrhagic disease in cattle. Six years elapsed between the first and last experiment. Shortly after the isolation of dicumarol, by the continuation of the brilliant work, a substance was synthesized that was identical in biological characteristics to the isolated principle. This substance is 3, 3′ methylenebis (4-hydroxycoumarin). The substance has the empirical formula $C_{19}H_{12}O_6$. It is optically inactive. There are two acidic hydroxyls in the molecules. The acidity of the pure substance falls between that of the phenols and carboxylic acids. A crystalling dimethyl ether $C_{19}H_{10}O_4(OCH_3)_2$ with M.P. 168–170° (physiologically inactive) has been prepared by methylation with diazomethane. In the pure state the substance has a low solubility in the ordinary organic solvents. It is insoluble in acid media. Basic solvents and dilute alkali effect solution readily and form salt. The substance could not be identified or characterized on the basis of its behavior toward the usual identification reagents. Its occurrence in nature has not previously been recorded. One and a half milligrams of the crystalline hemorrhagic agent causes approximately the same reduction in prothrombin level or activity of the plasma of standardized susceptible rabbits in forty hours as do 50 gm. of the standard spoiled-hay sample. Spoiled sweet-clover hay produced experimentally from melilotus alba and that found in agricultural practice contained approximately 0.003 per cent of the hemorrhagic agent on the dry substance basis. The overall yield of the substance in a fractionation scheme involving sixteen steps approximates 66 per cent of the quantity present.

The exact mode of action of dicumarol is not known. However, studies by Meyer *et al.* (37) and Bollman and Preston (6) of the Mayo Clinic have shown that dicumarol prolongs the prothrombin and coagulation time of the blood in animals, and Barker, Allen, and Waugh, also of the Mayo Clinic (1), have shown similar reactions in human beings. No harmful effects during or after the administration of the compound were found in dogs which were maintained for six weeks with from two to three times the normal amount of prothrombin. Continuous administration of excessive amounts of dicumarol produces in dogs a condition similar to that found in hemorrhagic sweet-clover disease. The prothrombin time of the blood and the bleeding tendencies may be partly controlled by transfusion of fresh whole blood. Vitamin K deficiency, inanition, or hepatic or renal injury greatly exaggerates the effect of this drug. The administration of large amounts of sulfathiazole does not alter the effectiveness of

dicumarol compound. The action of heparin is not prolonged when given to dicumarolized animals, and heparin is not involved in the action of dicumarol. The tendency toward thrombosis is demonstrated experimentally by thrombosis in glass or metal cannulas interposed in arteries or by thrombosis in occluded veins. This tendency is greatly reduced in animals that have prolonged prothrombin times due to the administration of dicumarol.

This effect of dicumarol is apparently, according to the opinion of some observers, the result of the suppression of the formation of prothrombin, and, as has been pointed out in the discussion of physiology of blood coagulation, prothrombin is one of the substances concerned in intravascular as well as extravascular coagulation of blood.

Considerable light has been thrown on this phase of the subject by a group of workers at the Mayo Clinic (1) who made studies particularly to determine the value of dicumarol in various clinical states. In so doing the drug was used on human beings. Dicumarol when administered orally prolongs the prothrombin time, impairs clot retraction, and increases the sedimentation rate of erythrocytes. Large amounts prolong the coagulation time. Hemorrhage may occur when dicumarol has greatly prolonged the prothrombin time. The drug seems essentially harmless otherwise. Dicumarol should be administered only when its effect can be determined by repeated calculations of the prothrombin time. The response of the prothrombin time of different patients is varied. In general, larger doses produce greater prolongation of prothrombin time than do smaller ones, and the effect endures longer. A plan of administering 300 mgm. on the first day, 200 mgm. on the second day, and 200 mgm. on each day after the second on which the prothrombin times is less than 35 seconds has been used by this group. However, other groups have used a plan of administering 300 mgm. daily until the prothrombin time has reached 35 seconds, and then administering 50 mgm. daily thereafter. Since the individual response varies so greatly at the present time, the plan of administration must be individualized and the individual dosage must be based upon the daily observation of the prothrombin time. A recent report by deTakats (13) further emphasizes this need of individualization in the administration of dicumarol. After the administration of the first dose, from twenty-four to forty-eight hours elapse before an effect on the prothrombin time is noted. In a few instances this time has been considerably longer. After discontinuation of administration, the prothrombin time may be prolonged from two days to from two to three weeks, according to the amount given. Heparin and dicumarol may be administered together when both quick and prolonged action are desired. The use of heparin is discontinued when the prothrombin time has been satisfactorily prolonged by dicumarol. Synthetic vitamin K has little or no effect on the prolongation of prothrombin time resulting from dicumarol. Transfusion of fresh blood will reduce for variable periods the prothrombin time which has been increased by dicumarol. It is determined from the reports of various workers discussing this phase of the subject and from our clinical experience that usually one 500 cc. transfusion is adequate to stop hemorrhage that may develop from dicumarol. If the drug is withdrawn and the transfusion is given, it is seldom necessary to repeat the transfusion. Usually the prothrombin drops immediately after the transfusion, but will rise again gradually without precipitating further bleeding. When the prothrombin time has reached 35 seconds it is safe to administer dicumarol again if its effect is desired for a longer period. Clinical and experimental studies strongly suggest the value of the administration of dicumarol in preventing intravascular thrombosis. The danger of hemorrhage from the administration of dicumarol serves as a constant emphasis for care in its use.

The routes of administration of dicumarol are discussed by Meyer, Bingham, and Axelrod (37). The use of 3,3′ methylenebis (4-hydroxycoumarin), oral or intravenous, cautiously carried out has not been attended by any symptoms of toxicity other than hemorrhage. Blood in microscopic quantities, as demonstrated by positive benzidine tests, appeared in the urine of 10 to 73 patients at the height of the response. In 4 patients occult blood was found in the stool by means of the guaiac test. In 1 operative case gross bleeding occurred after curettement of the uterus. Other groups have reported surgical procedures on patients under the influence of dicumarol without any untoward bleeding. We have had the same experience in our work.

The advantages of dicumarol as a possible substitute for heparin in the prevention of thromboses and in the treatment of thrombophlebitis and emboli are quite obvious. Dicumarol may be produced relatively cheaply. The cost of heparin in many instances is prohibitive of its use. Dicumarol may be given by mouth or intravenously as the disodium salt, and a prolonged effect is obtainable; whereas heparin usually requires continuous intravenous administration to maintain a constant anticoagulant effect. However, the re-

cent report of deTakats (13) infers that by the use of the heparin tolerance test we might be able to determine which patients may be maintained by the continuous intravenous administration as against the intermittent administration. The therapeutic index of dicumarol appears to be high. Doses as great as 25 mgm. per kgm. of body weight may be given intravenously to dogs without producing serious effects, whereas doses of 3 to 5 mgm. per kgm. will produce the desired prolongation of coagulation. It can be seen from this that the zone between the therapeutic dose and the lethal dose is great, which renders the drug safe when carefully administered. The inevitable latent period after the administration of dicumarol is a disadvantage in certain cases in which immediate prolongation of the coagulation time is desired. There is, however, no theoretical or clinical objection to immediate treatment with heparin, which produces an immediate anticoagulant effect, with subsequent substitution of dicumarol. This has been done quite satisfactorily by the various groups working with these agents and in our own practice. The probable additional disadvantages of dicumarol are the apparent greater toxicity in excessive doses and the fact that once coagulation is prolonged it cannot be shortened quickly by withholding the drug. The effect of heparin action ceases rather promptly after its administration is stopped. It has been pointed out, however, that one transfusion of fresh whole blood, from 300 to 600 cc., is usually effective in controlling bleeding tendencies produced by dicumarol and heparin. Dicumarol has been given in suitable doses orally each day for many weeks without discernible toxic effects. These observations have been confirmed by several groups of workers (1, 1a, 6, 14, 37).

Whether or not dicumarol or one of its derivatives will be as efficacious as heparin appears to be in preventing thrombosis is still to be determined. However, recent reports by Barker, Allen, and Waugh (1a) at the Mayo Clinic, referred to earlier in this paper, and the results of other groups indicate that dicumarol is efficacious for this purpose. It has been given for the purpose of preventing thromboses and for the treatment of established thromboses. The indications are that it is of definite value (1, 14, 22, 23).

Dicumarol is potentially capable of inducing undesirable hemorrhage even in a dosage which is considered to be within therapeutic range. It is the firm belief of Meyer *et al.* that its indiscriminate use would be extremely hazardous, and they urge that those who employ it administer the minimal effective dose and avoid its use when gross hepatic disease is known to exist. Because of the considerable individual variation in response, it is imperative for the present that the prothrombin and coagulation times be measured not less often than once a day. The desired degree of prolongation of coagulation is not known with certainty, but it appears that a coagulation time of from fifteen to twenty minutes should be suitable and not too hazardous. The prolongation of the prothrombin time to between twelve and one-half and nineteen seconds (approximately 50 to 25 per cent of the normal) is probably reasonably safe. At the nineteen-second level the percentage of prothrombin in the blood according to the method used by Meyer *et al.* is approximately 25 per cent, and lower levels are not desired. The actual prothrombin time figures by other groups are between thirty-five and sixty seconds. If the prothrombin time is thirty-five seconds or above on any given day, the dicumarol is withheld until the prothrombin time falls to thirty-five seconds or below (1–37).

It is not established beyond question whether or not the coagulation time is prolonged because of the decrease in prothrombin, although there is, in most instances, a parallelism between these two factors. The manner in which the dicumarol acts to produce the prolongation in prothrombin time after the latent period is not definitely known. The theory that seems most attractive is that it acts as a physiological inhibitor of prothrombin formation by the liver and that during the latent period prothrombin of the blood is depleted. This theory of liver inhibition is strengthened by the fact that vitamin K administration in adequate dosage is ineffective in preventing the increase in prothrombin time.

A second possibility is that the prothrombin produced in the presence of the hemorrhagic agent is altered in such a way that it is inactivated. The latent period might be due to some change that the dicumarol must undergo in the body during the latent period before it is capable of functioning. Meyer (37) states that studies are in progress by W. R. Sullivan, R. S. Overman, M. A. Stahmann, and K. P. Link, which indicate that the hemorrhagic action takes place after the molecule of the compound has undergone certain changes in the body. Meyer *et al.* conclude that:

1. Dicumarol given to human beings produces prolongation in the prothrombin time and coagulation time.

2. The minimal effective dose should be employed. This dose varies with each individual. It appears that the initial dose of 5 mgm. per kgm. with subsequent daily oral doses of from 1 to

1½ mgm. per kgm. is effective in most patients. A single intravenous dose of 4 mgm. per kgm. was found to be suitable and effective. This dose may be repeated when necessary.

3. During the period of observation, the prothrombin time and the coagulation time should be determined not less often than once daily. If the prothrombin time becomes too great the dicumarol should be withheld temporarily. Blood transfusions of from 300 to 600 cc. are effective in controlling bleeding.

4. No gross toxic effects other than bleeding in one patient following curettage of the uterus attended the use of dicumarol.

5. Administration of vitamin K did not prohibit or correct the prothrombin deficiency produced by dicumarol.

Alfred Blalock, writing in *Surgery* (5) in 1939, states that it must be determined whether or not heparin interferes with the healing of incisions and with the normal responses of the body to infection. Laufman and Heller in Chicago (21) recently have thrown considerable light on this question. In working out this problem they used 80 dogs in the experiment. The animals were given heparin and the strength of their wounds was tested at varying postoperative periods. It was concluded that there was some slight effect on wound healing up to the fourth postoperative day, but thereafter no effect on wound healing could be attributed to the administration of heparin. Furthermore none of the groups working with heparin or dicumarol have been able to find any interference by these agents with the normal responses of the body to infection.

Contraindications to the use of these agents have been established by the groups working at the Mayo Clinic and by J. Lehman of Sweden (1, 1a, 6, 22). They are in brief:

1. Renal insufficiency.

2. Severe heart disease (especially cardiosclerosis).

3. Hypertonia.

4. Obstructive jaundice.

5. Bleeding in pregnancy and in the puerperium or bleeding from any other cause.

6. Suspected or diagnosed vitamin C deficiency should be treated along with the administration of dicumarol.

CLINICAL APPLICATION

We will present a summary of some of the representative reports of the clinical applications of these anticoagulant agents, mentioning some of the experimental work that has led directly to the clinical applications of heparin and dicumarol.

Laufman (20), reporting on the use of heparin experimentally in reference to mesenteric thrombosis, used several dogs in which he strangulated varying lengths of the loops of the bowel and administered heparin; he then studied the effect of heparin in relation to the amount of bowel involved in mesenteric thrombosis and to the stage of viability, and the effect with or without resection. He concludes that it is unsafe to administer heparin after impairment of circulation of the intestine when resection is not performed, although it appears that heparin enhances the chances of recovery of short devascularized segments. In cases of more extensive mesenteric vascular occlusion or strangulation, it should be reserved only for cases in which resection is performed.

Jorgen Lehman (22) conducted some experiments with rabbits and also administered dicumarol to human subjects to produce hypoprothrombinemia with the view of preventing postoperative thrombosis or benefiting established thrombosis. Extensive experiments by this worker showed that dicumarol produced a reproducible and reversible hypoprothrombinemia, the prothrombin index (Quick) being lowered to from 10 to 20 for one or two days by a single dose by mouth of from 3 to 4 mgm. per kgm. Keeping the prothrombin index at from 10 to 40 of normal prothrombin for a month did not act deleteriously on the restoration of normal prothrombin values after discontinuation of dicumarol. Lehman found that no toxic effects could be observed on the circulation, respiration, intestines, liver, kidney, heart, or the per kgm. of body weight (rabbits). He concludes that dicumarol in nonlethal doses produces a specific reversible inhibition of the formation of prothrombin and has little toxic effect. He also found that the effect of dicumarol was not antagonized by synthetic vitamin K, but that blood transfusions were able to elevate the prothrombin in from three to five hours. Lehman shows that prothrombin resistance is higher in individuals with a tendency to thrombosis than in normal individuals. When an initial deep fall in the prothrombin index to about 20 to 30 was accomplished a well marked improvement was seen in the patients with thrombophlebitis, which was demonstrated by a fall in temperature, diminished swelling of the leg, and objective amelioration of their condition. In no cases did the thrombosis spread after the fall in prothrombin, but in 2 cases there was a spread before the fall in prothrombin. Bauer has used heparin in the treatment of thrombosis (3). He maintains the diagnosis should be definitely established before the administration of heparin. Phlebography is used

to insure early diagnosis. Heparin is given in large doses as soon as the diagnosis is established. The plan of administration was generally 100 mgm., three times daily, for from three to five days, the total dosage averaging 1,100 mgm. in the cases in which the thrombotic process was still localized in the lower leg. In the cases in which the thrombotic process had spread to the thigh, the dosage was somewhat larger, the total averaging 1,540 mgm. The disease generally follows an abortive course. The patients treated with heparin had no complications and were able to leave bed in a few days. By the use of heparin the treatment time for patients suffering from thrombosis was reduced by about 1/7th of that usually required. The mortality from thrombosis was greatly reduced, and, subsequently, serious invalidism will probably be much decreased.

Priestley and Barker, reporting on postoperative thrombosis and embolism, summarize their experience with the administration of heparin to 63 patients (40). They discuss the administration of heparin, its indications, and their clinical experience. They present the following interesting summary:

"Pulmonary embolism in our experience is responsible for approximately 6 per cent of deaths which occur after major surgical procedures. A number of factors influence the likelihood that embolus or thrombosis will follow any operation, and these include site of the operation, magnitude of the procedure, presence of infection or malignancy, diseases of the blood or cardiovascular system, obesity, age, and sex. The majority of all thromboembolic phenomena occur within the first two weeks after operation. Approximately one in four cases of pulmonary embolism is associated with clinical evidence of thrombophlebitis, and similarly, approximately one in four cases of thrombophlebitis is associated with evidence of embolism. Of all patients who experience pulmonary emboli approximately one half have a single nonfatal embolus, one quarter have a single fatal embolus, and the one quarter remaining have multiple emboli which in approximately 60% of cases are followed finally by fatal embolism. Proper use of heparin in all cases in which evidence of nonfatal pulmonary embolism is available should prevent about one third of the deaths which now occur from postoperative pulmonary embolism."

G. Murray, of Toronto, and his coworkers probably have more clinical experience than anyone else in the use of heparin (30, 31, 32, 35, 36). Reference to their work gives excellent knowledge in regard to the indications for, clinical applications of, and results following, the use of heparin. Murray and MacKenzie (33), presenting a review of the treatment of established thrombosis and its complications, report the study of a series of 877 cases of thrombophlebitis. By way of preface to this report they state that postoperative embolism is a common and dangerous complication. According to post-mortem records at the Toronto General Hospital (19) over 10 per cent of all deaths in this hospital are due to this disease, and in 20 per cent of all post-mortem examinations pulmonary emboli are found. In an attempt to find some way to overcome this disease, experimental work was started at the University of Toronto in 1929 and is still in progress. They have reported some very striking results with the prophylactic and therapeutic use of heparin as indicated in the given references. Also Murray (32) has recently reported (36) 5 successful abdominal aortic embolectomies made possible by the use of heparin.

In a recent editorial, DeBakey (11), taking a conservative and somewhat antagonistic attitude toward these agents, discusses dicumarol and prophylactic anticoagulants in intravascular thrombosis. He recalls the intensive studies that have been undertaken to determine the pharmacological and therapeutic action of dicumarol. He reviews the modes of action of heparin and dicumarol and weighs the advantages and disadvantages of these agents, which have been summarized, and further introduces several considerations to support the caution shown by the provisional reluctance to accept the conclusions of several groups of workers from their observations in experimental studies in which these agents had been administered for the prevention of intravascular thrombosis. "Notwithstanding certain implications the statistical significance of the reported results upon which many of the conclusions are based is open to question because the series of investigation is not adequate nor are the results sufficiently impressive to justify definite statements. This is clearly demonstrated by a comparison with other incidences of postoperative thrombosis in cases not receiving anticoagulant prophylactic measures. Thus, in a series of 4,410 consecutive operations performed at the Charity Hospital in New Orleans, exclusive of procedures on the eyes, ears, nose, and throat, there were only three (or 0.06%) cases of postoperative thrombophlebitis. Even more significant is the fact that better results have been reported following the use of much simpler, safer, and more economical prophylactic measures than the administration of dicumarol or other anticoagulant agents. Thus, Zava, using

early ambulation postoperatively, reported over 6,000 surgical cases, many of which were gynecologic, without a single occurrence of embolism. In addition to these considerations is the fact that dicumarol, like other anticoagulants, possesses certain hazardous features."

At this point DeBakey mentions the hazardous features and contraindications of dicumarol which have been given. He gives his considerations as to why he feels that, for the present, dicumarol cannot be regarded as a safe, efficacious, and satisfactory prophylactic or therapeutic agent in intravascular thrombosis. "In the prophylaxis and treatment of intravascular thrombosis certain difficulties and objectionable features must be overcome before any anticoagulant can be considered entirely satisfactory and its use become widely adopted. The prophylactic value of any anticoagulant agent is manifestly difficult to establish in such notoriously unpredictable conditions as intravascular thrombosis. Further emphasis is placed upon the undesirability of this particular characteristic by the fact that the anticoagulant agent must be employed in all cases, which is obviously impractical. This is especially true in view of the danger of hemorrhage which may follow the use of an anticoagulant agent and which assumes obvious significance in surgical cases. Therapeutically the use of an anticoagulant in intravascular thrombosis has at least the theoretical objection of increasing the tendency of embolism. That this is not entirely theoretic, however, is shown by our experience with a patient, who, while heparinized over a period of four weeks, had five nonfatal emboli. Obviously in such cases the more certain means of preventing propagation of the thrombus or embolization is by proximal vein ligation. In view of the present lack of trenchant knowledge concerning the etiologic factors in intravascular thrombosis the rationale of anticoagulants as combative measures may be justifiably questioned. These protesting considerations to the prophylactic and therapeutic use of all anticoagulants in intravascular thromboses are not intended as critical disapprobation, but rather as criticism in its strict etymologic sense, that is, evaluation. A restatement of facts is frequently necessary to dispel the fog of enthusiasm and thus permit a clear discernment of objectives."

As DeBakey infers at the conclusion of these considerations, these protests are made in part to arouse interest, and stimulate discussion and further investigation of these anticoagulants which definitely have a very important place in the prophylactic and therapeutic armamentarium of the medical profession in combating the problems of thrombosis and embolism, but about which we have much to learn as yet.

In contrast to this conservative viewpoint, it is interesting to review the reports of several of the groups of workers referred to, particularly the enthusiastic conclusions drawn by Barker, Allen, and Waugh of the Mayo Clinic (1a), the quite promising results obtained by Evans of the Lahey Clinic (14), and the excellent results reported by J. Lehman of Sweden (23), on the use of anticoagulants, especially the use of dicumarol in the prevention of postoperative thrombophlebitis and pulmonary embolism. Also, Bauer, by the use of heparin, has reduced the treatment time for patients suffering with thrombosis to one-seventh of that usually required. His mortality from thrombosis was greatly reduced. These workers have not given these drugs at random but have picked the patients most likely to become victims of these unfortunate circumstances (thrombophlebitis and embolism), and the consensus is that adequate elevation of the prothrombin time by means of administration of dicumarol by mouth to postoperative patients is apparently effective in preventing postoperative thrombophlebitis and pulmonary embolism. The drug is administered according to the plan described. Precautions are stressed. All groups emphasize that at present it is unwise to give dicumarol unless the prothrombin time can be determined accurately each day. There is some risk of bleeding in postoperative cases when dicumarol is given, but this risk is comparatively small.

CLINICAL REPORT

Since 1939 we have administered heparin to 21 patients in our work at the Pfeiffer Surgical Clinic. During the past year we have used dicumarol or a combination of heparin and dicumarol on a half dozen patients. The series of cases is not large, but it is indicative of the value of this agent as confirmed by the many groups reporting larger series. Heparin has been administered for prophylactic and therapeutic indications. It is true that there have been several cases in which we could claim little prophylactic benefit and little therapeutic value. On the other hand, there have been several cases in which we could see outstanding therapeutic value, and from the preventive point of view we have believed that definite good has been obtained from the administration of heparin and, more lately, of dicumarol. We will mention briefly the cases in which we could claim no value from the administration of these drugs either because of the unconquerable disease or because of the lack of accomplishment of purpose.

We will also report briefly a few cases in which we feel outstanding results have been obtained.

Heparin was used in several cases of peripheral vascular disease, particularly embolism associated with hypertensive cardiovascular disease and arteriosclerosis, in which the progress of the embolic phenomena was not stayed. Because of the progression of the vascular occlusion, amputation followed in several instances. In these cases the patients were seen later than twenty-four hours after the onset of the vascular accident, the administration of heparin thereby being delayed, which rendered its failure more likely. Heparin was administered in 1 case of embolectomy. It was a saddle embolus at the bifurcation of the abdominal aorta. Embolectomy was performed successfully by Pfeiffer. Heparin was administered, but the patient died about twenty-four hours later from heart failure secondary to rheumatic heart disease of long standing. However, the circulation had returned to the lower extremities as effectively as it was generally. The patient lived long enough to prove that heparin prevented the occurrence of thrombosis at the site of operation. Another patient, age thirteen, received a severe gunshot wound of both thighs which destroyed a section of one femoral artery and produced extensive destruction of the muscle of the opposite thigh without destruction of the circulation in this extremity. The injured femoral artery was repaired by Pfeiffer, who grafted a section of the long saphenous vein and thereby successfully restored the circulation to the extremity. The patient died within twenty-four hours after the operation from a blood-stream infection with gas bacilli, despite the use of gas antitoxin. However, the patient lived long enough to prove that thrombosis at the operative site was prevented by heparin, as was shown at the post-mortem examination. As long as the patient lived adequate circulation was maintained in the extremity, and at post mortem the lining of the entire vessel, including the proximal and distal portions where the saphenous vein had been sutured, was entirely free of any evidence of thrombosis.

Another classical clinical case of mesenteric thrombosis was given heparin; the patient, a middle-aged Italian woman, recovered completely without further complication.

An elderly man who was suffering from chronic heart disease and was admitted to the surgical service with the diagnosis of acute surgical abdomen was explored and found to have mesenteric thrombosis of the terminal ileum. The circulation was impaired to approximately 18 in. of the terminal ileum. The patient's abdomen was closed without intestinal resection. Heparin was administered for its immediate effect as an anticoagulant and dicumarol was given immediately also. As soon as the prothrombin time was above thirty-five seconds the administration of heparin was discontinued. The patient made an uneventful recovery and returned to his usual status of health. This case is particularly interesting from the point of view that mesenteric thrombosis carries a very high mortality rate. Mesenteric thrombosis is usually progressive and fatal.

Several cases of thrombophlebitis were treated with heparin and dicumarol. Venous ligations were performed with the prothrombin time above thirty-five seconds without any undue technical difficulty in producing hemostasis. In these cases we confirm the belief of Evans, Bauer, J. Lehman, and others that the course of the disease is shortened, and therefore the period of suffering and disability from these vascular diseases are shortened.

Sensitivity reactions of antiphylactic nature occurred in 3 patients. However, when the batch of heparin was changed the reactions did not occur in the same patients; therefore it was concluded that they were caused by impure heparin.

Bleeding occurred in 1 case and was definitely due to overdosage. On a given day the drug was administered despite the fact that the prothrombin time, which was above thirty-five seconds on this day, had not been checked. Consequently the patient developed bleeding from the mucous membranes of the nose and mouth, hemoptysis, and hematuria. The bleeding ceased rather promptly following the administration of 500 cc. of fresh whole blood. Although the prothrombin time remained high for several days, bleeding did not recur. The patient made a prompt and uneventful recovery from postoperative thrombophlebitis.

A group of workers at the Mayo Clinic (1a), in conjecturing on the benefits to man of artificially impaired coagulation of the blood, review briefly the evidence from both clinical and experimental observations, which is now conclusive and a matter of medical record, and state that if physicians can reduce the coagulation of blood safely over long periods of time it is to be expected that the following conditions can be prevented:

1. Thrombosis of the coronary arteries
2. Thrombosis of the cerebral arteries
3. Thrombosis of thrombophlebitis
4. Pulmonary embolism
5. Thrombosis of arteriosclerosis obliterans
6. Thrombosis of thromboangiitis obliterans
7. Peripheral arterial embolism
8. Venous thrombosis of noninflammatory origin as in polycythemia vera.

SUMMARY

In brief we will summarize the most important clinical conditions to which anticoagulant prophylaxis and therapy have been applied:

1. Prophylaxis
   a. After operations that are more commonly followed by thrombosis and embolism
      (1) Splenectomy
      (2) Malignancy
      (3) Pelvic operation
      (4) Hernia
   b. Prevention of peritoneal adhesions
2. Surgery of the blood vessels
   a. Traumatic injuries
   b. Thrombosis and embolism—surgical removal
3. Therapy
   a. Vessels of the extremities
      (1) Phlebitis and thrombophlebitis
      (2) Phlebothrombosis
      (3) Phlegmasia alba dolens
   b. Pulmonary vessels
   c. Central retinal vein
   d. Coronary vessels
   e. Mesenteric vessels
   f. Cerebral vessels
4. Blood transfusions (15)
5. Laboratory work

Indications, advantages, disadvantages, and future possibilities of anticoagulants have been discussed. Further problems are to be worked out, particularly those of indications and dosages.

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ABSTRACTS OF CURRENT LITERATURE

SURGERY OF THE HEAD AND NECK

HEAD

Dandy, W. E.: An Operation for Scaphocephaly.
Arch. Surg., 1943, 47: 247.

Various operations for scaphocephaly have been devised in order to allow the expanding brain free room for development. The pathological basis of the condition is premature synostosis. The author has devised a plan by which a large piece of bone is elevated, first on the right side of the head, and then, at another operation, another piece of bone is elevated on the opposite side of the head. These bone flaps are hinged in the manner illustrated in the figure.

The case which is described was that of an infant five months old, and the result of the operations appeared to be entirely satisfactory.

ADRIEN VERBRUGGHEN, M.D.

Fig. 2. Photographs taken six months after the first operation showing front and top views of a patient treated by the method described in this article.

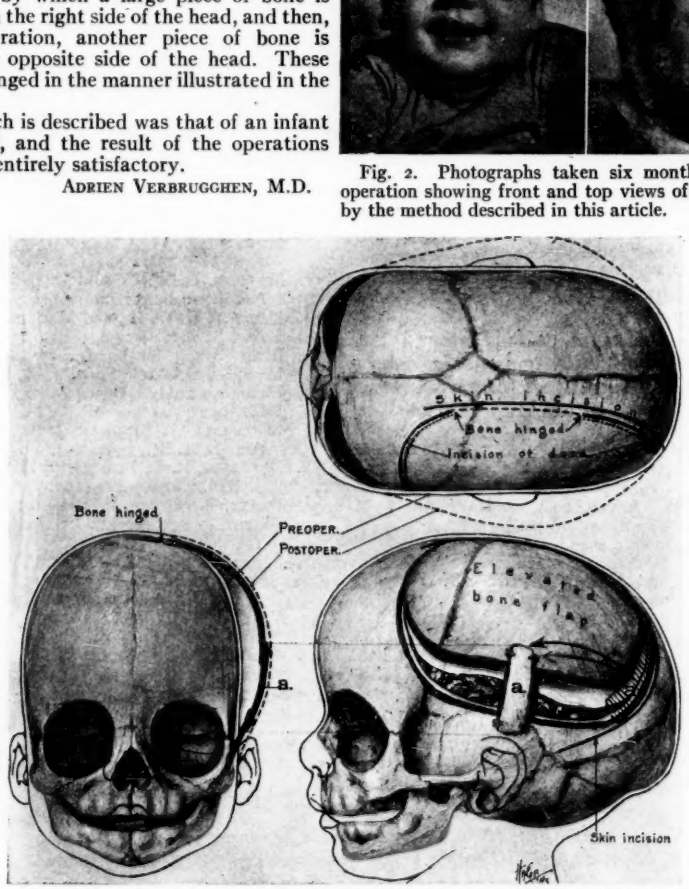

Fig. 1. Drawing of the operative procedure for correction of scaphocephaly. The narrow head is enlarged by elevating a large bone flap on each side and holding it in position by a transplant of bone (from the bone flap). The dura is incised to allow the brain to expand. The same procedure is carried out on the opposite side two or three weeks later.

Converse, J. M.: Some Aspects of Emergency Plastic Surgery in War Injuries of the Face. *Ann. Otol. Rhinol.*, 1943, 52: 637.

The plastic surgeon, assisted by a dental surgeon experienced in maxillofacial prosthesis, is best qualified to treat facial injuries. Multiple facial lacerations and wounds are caused by missiles, such as stones and gravel, glass, pieces of brick, and cement, set in motion by the blast of shells or bombs. These missiles constituted the most frequent cause of facial disfigurement in the civilian bombing casualties in England. The high speed missiles create irregular, jagged, contused wounds out of proportion with their size. Avulsion of the nose, lips, or whole cheek is seen, but seldom in the living patient as the patient rarely recovers from the serious pulmonary or intracranial lesions. Crushing injuries are frequently caused by falling building materials. "Crash" injuries are found in airplane, tank, motorcycle, and "jeep" accidents. The bony protuberances of the face, the supraorbital ridges, nasal bones, malar bones, and chin act as "bumpers" and receive the first impact. Burns constitute one of the most frequent and most serious problems of modern mechanized warfare and the face is unprotected by clothing.

The aim of the surgeon treating any facial injury is the prevention and treatment of deformity and the restoration of function. The face differs from the rest of the body because it is the medium of individual expression and identity and it is remarkably resistant to infection. Fragments of fractured facial bones should be preserved unless they are completely detached; where wound closure cannot be accomplished without tension, local plastic flaps must be made to relieve tension or else a primary skin graft should be used. The most practical treatment of facial burns appears to be the application of the sulfonamide ointment after the cleansing of the areas. The treatment of third-degree burns is based upon the early replacement of the destroyed skin by skin grafting. It is preferable to wait until around the tenth day.

In cases of severe maxillofacial or frontal injuries with cerebrospinal fluid leak or dural tear, meningitis and facial injury are the primary problems. These can be treated by (1) doing nothing, (2) treating the facial fracture and hoping the cerebrospinal rhinorrhea will stop, or (3) closing the dural opening through a frontal flap and reducing the facial fractures. A careful evaluation of each case is necessary. Air in the ventricles or frontal bone in the brain are indications for operation. LOUIS T. BYARS, M.D.

EYE

Ballantyne, A. J.: Ocular Manifestations of Spontaneous Subarachnoid Hemorrhage. *Brit. J. Ophth.*, 1943, 27: 383.

The author reports 5 fatal cases of spontaneous nontraumatic subarachnoid hemorrhage and describes the ocular manifestations and the mode of development of hemorrhages in this condition. Hemorrhage from the circle of Willis usually results from rupture of an aneurysm or of a weakened vessel wall and is associated with intense deeply seated pain often accompanied by paresis of one or more ocular muscles. Severe cases are characterized by sudden onset and signs suggestive of cerebral compression and meningeal irritation, such as pupillary disturbances, nystagmus, conjugate deviation of the eyes, paralysis of cranial nerves, hemorrhages in the retina, papilledema, and the presence of blood in the cerebrospinal fluid. Hemorrhages occur simultaneously and independently at many places, that is, they are scattered and have no continuity.

These multiple hemorrhages are attributed to a sudden rise of the intracranial pressure which causes stasis in all the venous channels which drain the tissues of the eye and the contents of the orbit. It is pointed out that the blood in the cerebral subarachnoid space does not travel through the optic foramen into the subarachnoid space of the optic nerve, but that the blood in the dural sheath at the apex of the orbit passes forward into the subdural and subarachnoid space and by pressure and tension on the central retinal vein causes stasis in the central retinal vein with resultant hemorrhages in the retina and vitreous. Some of the clinical signs of subarachnoid hemorrhage, such as oculomotor paresis and disturbance of the conjugate movements result from hemorrhages in the midbrain. JOSHUA ZUCKERMAN, M.D.

McGregor, I. S., and Hill, J.: Reticulin Content and Prognosis in Melanoma of the Uvea. *Arch. Ophth.*, Chic., 1943, 30: 291.

The authors discuss the prognostic value of the reticulin content in malignant melanoma of the uvea. They investigated a series of 82 cases over a period of twenty years, from which unequivocal histories and histological examinations of specimens were obtained in 41 cases. The average period of survival was approximately eight years.

With few exceptions a fuller reticulin picture was presented by the patients who survived from six to fifteen years than by those who lived six years. Moreover, with few exceptions the longer-lived group presented a predominance of the benign spindle A, or A and B type of cell; and the shorter-lived group presented a predominance of mixed and epithelioid types, and an increased pigment content.

The authors agree with Callender and Wilder, who found that the spindle-cell types were relatively benign and that a full reticulin content was a favorable sign, while epithelioid and mixed-cell types and a poor reticulin content were unfavorable signs.

JOSHUA ZUCKERMAN, M.D.

EAR

Guggenheim, L.: Therapy of Deafness. Report of Cases. *Laryngoscope*, 1943, 53: 503.

Over 50 per cent of the 18,000,000 deafened in the United States owe their affliction to tympanal path-

ology resulting from obstruction of the eustachian tubes in early life, and this is due to inadequate removal of adenoid tissue and to the retention of embryological mesenchyme. Failure of the mesenchyme to absorb is often associated with exuberant lymphoid masses in the nasopharynx. Persistent mesenchyme means inadequate drainage and susceptibility to tympanal infection. The so-called catarrhal condition of the ear is the result of adhesive processes brought about by the differentiation of mesenchyme into connective tissue.

The author describes his technique for direct adenoidectomy and dilatation of the eustachian tube with a Gerjoye dilator. JOHN F. DELPH, M.D.

MOUTH

Higley, L. B.: The Proper Time to Begin Orthodontic Treatment. *J. Am. Dent. Ass.*, 1943, 30: 1329.

This article, in the main, presents the results of a critical analysis of the contentions of Hellman relative to the time at which orthodontic treatment should be inaugurated.

The author recommends early treatment or "aid," believing that guiding the dentofacial development to adult efficiency by preventive methods is better than simply waiting until damage is done and then correcting the deformity.

Evidence in favor of early treatment is given.

WILLIAM G. SKILLEN, D.D.S.

NECK

Mitchell, H. E.: Tumors of the Larynx. A Review of 105 Cases. *Laryngoscope*, 1943, 53: 457.

The author reviews 105 cases of tumors of the larynx which consisted of 83 malignant tumors, 1 of doubtful malignancy, and 21 benign tumors. The ratio of malignant to benign tumors in adults was approximately 5½ to 1. There was only 1 woman among the 83 patients with carcinoma. The highest age incidence of carcinoma was between fifty and sixty years, and 90 per cent of the patients were between forty and seventy years of age. The patients with benign tumors were, on the whole, younger.

The diagnosis of carcinoma is made from the history and physical examination. Hoarseness was the most persistent symptom of both malignant and benign lesions. A pathological diagnosis is essential since some apparently benign lesions show malignant changes. Nor should one biopsy be considered sufficient if the pathologist reports a benign lesion when clinically it appears malignant.

Squamous-cell carcinoma was the most frequent lesion in this series, as in other reported series; there were 62 cases.

The treatment of carcinoma of the larynx should be surgical whenever the extent of the lesion will permit operation. In early, intrinsic cancer of the larynx, laryngectomy usually is preferable, although laryngofissure may suffice in properly selected cases. In cases of extensive lesions, often only irradiation and palliative procedures may be employed. In the author's reported series of 83 cases of carcinoma only 11 patients had a lesion so limited that laryngectomy was justified. Of these 11, 6 are alive and well: 1 for ten years, and 1 each for four and one-half years, three years, two years, one and a half years, and fourteen months.

Of the 4 patients having laryngofissure, 2 are alive and well five and a half years after operation. The other 2 had advanced lesions and died within seven months of the operation. Twenty-seven cases required tracheotomy—often as an emergency measure.

The author concludes that since only 15 of 83 patients with laryngeal carcinoma were in a condition to warrant laryngeal operation the results do not depend primarily on improvements of surgical technique. The general results of treatment of carcinoma of the larynx will not markedly improve until patients are seen earlier in the course of the disease. EARL O. LATIMER, M.D.

McCall, J. W.: Preliminary Voice Training for Laryngectomy. *Arch. Otolar.*, Chic., 1943, 38: 10.

The value of preliminary voice training for laryngectomized patients is shown by the author's report on 32 cases in which laryngectomy was performed for carcinoma of the larynx at St. Luke's Hospital, Cleveland, during the period from 1936 to 1942. Of 19 patients who had no preliminary training for development of the esophageal voice, only 3 acquired the ability to speak after operation. Of the 13 who had preliminary training, all developed the ability to speak well enough to be heard over the telephone, and several of these patients had excellent voices.

Patients who are to be subjected to total laryngectomy should have voice training before, not after, the operation for the following reasons: (1) the development of an esophageal voice is dependent on the patient's ability to belch; (2) it is much easier to learn to belch before the larynx is removed than after; and (3) the time required to master the technique of belching is short (one week to ten days) and does not jeopardize the patient's chance of survival. NOAH D. FABRICANT, M.D.

SURGERY OF THE NERVOUS SYSTEM

BRAIN AND ITS COVERINGS; CRANIAL NERVES

Rahm, W. E., Jr., and Scarff, J. E.: Electrical Excitation of the Cerebral Cortex; Description of a New Stimulator. *Arch. Neur. Psychiat.*, Chic., 1943, 50: 183.

The use of electrical stimulation of the cerebral cortex in the study of neurophysiology was first reported in 1870 by Fritsch and Hitzig. This work was done by the use of the simple galvanic current. In 1873 Ferrier reported on a similar work with the use of the faradic current.

Barthalow of Cincinnati in 1874 was the first to study the human brain by means of the electrical current using faradic stimulation. This was done by inserting needles through a cancer which had eroded the skull. Although Dana repeated a similar study in 1893, Sir Victor Horsley in the meantime had stimulated the exposed cortex at the operating table.

The different types of stimulation that have been used have been obtained with the galvanic, faradic, and modern alternating currents, the inductorium, and the simple thyratron stimulator. A circuit diagram and the type of wave produced by each current is shown in the article.

The authors present their new modified type of thyratron stimulator as devised by Rahm and used clinically by Scarff. A description, diagram, and discussion is presented, but this can best be studied by referring to the article. "While the simple thyratron marks a great advance in the technic of physiologic electrical excitation, it is still not without considerable possibility of error when precise quantitation of strength and rate of stimulation is desired."

JACK I. WOOLF, M.D.

Boldrey, E.: The Pathology of Brain Tumors and Its Relationship to Roentgenological Diagnosis. *Radiology*, 1943, 41: 107.

An attempt is made to correlate the pathological and roentgenological characteristics of brain tumors. First to be considered is the supratentorial group. Gliomas constitute between 40 and 50 per cent of all tumors of the central nervous system, and of the supratentorial group glioblastoma multiforme is by far the most common. Despite their rapidity of growth, calcification is not unusual and bone formation may be encountered. To the radiologist all gliomas have much in common. All may give signs of cerebral tumefaction. None is truly encapsulated, nor has any one of them a gross characteristic which can be said to be strictly peculiar to it. Focal changes in the skull are rare. Large cysts are commonly seen in the pilose and gemistocytic types of astrocytomas but not in the astrocytoma diffusum. Any tumor of the glioma group may exhibit calcification, but calcification may be especially dense in astrocytomas of the pilose or gemistocytic types. On the basis of probability, calcification is more suggestive of astrocytoma than of any other tumor. In the other gliomas the radiopaque material is usually more nebulous, often being observed only by stereoscopic study. Pneumographic studies of patients with supratentorial gliomas usually show a generalized as well as a localized ventricular shift because of hemispheral edema. This is especially marked in glioblastoma multiforme. Tumors within the lateral ventricle are likely to be ependymomas, although intraventricular projections of other types are not rare.

From the roentgenographic standpoint the pathological picture of meningeal fibroblastoma resolves itself into 5 subdivisions related to the pathological subtypes of Cushing and Eisenhardt. In Type I there have been invasion and destruction of the overlying skull so that there is a thickening of bone about a central core of complete neoplastic osseous destruction. Type II is made up of that group in which the arachnoidal cells have traversed the dura, invaded the canals of the skull, and spread out beneath the galea. In the roentgenogram the skull appears wormeaten but there is sufficient bony framework to function anatomically as a cranium. Type III shows simple proliferative reaction of the two tables to the neoplastic inroads into the haversian canals. The fusiform thickening with perpendicular bony spicules and radiographic preservation of the original tables constitute the pathological picture. In type IV the inner table alone may respond to the adjacent meningeal tumor. This reaction has been noted particularly near the midline of the anterior fossa in the base of the skull. The homogeneous osteomalike projections may be ivory-hard. Type V shows no bony thickening in the roentgenogram and at most there is but a deepened or prominent vascular channel. Type V comprises nearly half of the meningeal fibroblastomas. Focal ventricular distortion is rare; usually there is some displacement of an entire section of the ventricular system.

Miscellaneous supratentorial tumors include the group about the sella. The roentgenogram of chromophobe adenomas is that of direct pressure on the sella, especially on the dorsum and the floor. There may be undercutting of the tuberculum sellae with increase of the sagittal dimension of the sella. Eosinophile adenoma produces the characteristic changes of acromegaly, while basophilic adenoma has no characteristic x-ray appearance. In a person whose skeletal age is definitely less than his chronological age, or whose development is infantile, a roentgen picture of an expanded sella with erosion of the dorsum suggests craniopharyngioma. The presence of calcium in the suprasellar region in addition is almost pathognomonic. A benign cyst of the

third ventricle may be outlined in the pneumogram. A neoplasm at the back of the third ventricle, especially one with calcium demonstrable in the x-ray film, suggests a pineal tumor. The principal roentgenological characteristic of angioma is a tendency toward deposition of calcium in the walls of the vessels and surrounding tissues.

Of the subtentorial tumors, medulloblastoma is the most common glioma and the most common tumor of this region in childhood. It is difficult to observe calcification in lesions of the posterior fossa because of the superimposed mastoid processes and air cells. Ventriculography yields valuable diagnostic information in these cases. When the aqueduct and upper part of the fourth ventricle are displaced forward the tumor must arise posteriorly, and it is then most commonly a medulloblastoma if the patient is a child, or an astrocytoma if the patient is older. If the ventricle is pushed forward and to one side, further weight is added to the diagnosis of astrocytoma, since this tumor is more common in the hemispheres. When there is evidence of a tumor arising from the floor of the fourth ventricle the possibility of an ependymoma is strong. A smoothly outlined retrograde curve of the floor of the fourth ventricle with widening of the space between the floor and the cisterna pontis suggests a tumor of the pons, often a spongioblastoma. When tumor of the cerebellopontine angle is suspected it has been customary to attempt the demonstration of comparative enlargement of the internal auditory meatus. In many patients no difference can be demonstrated, and such a procedure may cause trouble. Pneumography is not always necessary, but when used, displacement of the fourth ventricle and aqueduct laterally to the opposite side may be demonstrated.

With respect to other intracranial growths, x-ray demonstration of erosion of the basiocciput and basisphenoid, or pneumographic evidence of an intracranial mass arising from the clivus strongly suggests chordoma when the clinical findings are compatible. Attention is called to the tendency for metastatic tumors to be located where the internal carotid artery gives off tiny branches to the gasserian ganglion, the sphenoid bone, and the adjacent meninges. Erosion of the skull in this vicinity usually suggests the diagnosis. Similar erosion may occur in intracranial aneurysm, in which case the vascular fault may be demonstrated by arteriography. JOHN L. LINDQUIST, M.D.

Abbott, K. H., and Adson, A. W.: Primary Intracranial Lymphosarcoma: A Report of 2 Cases and Review of the Literature. *Arch. Surg.*, 1943, 47: 147.

Reports are given of what appear to have been 2 primary lymphosarcomas of the intracranial dura mater, the one occurring in a man and the other in a woman, aged twenty-four and fifty-seven years, respectively. A third case is mentioned as a possible example of this type of tumor, since to date there is only surgical confirmation of its belonging to this group. Although the possibility that the tumors may have originated in cranial bone cannot be ruled out, the facts that erosion was greater in the inner table than in the outer and that most of the tumor was in the dura mater are arguments in favor of a dural origin.

Cloward, R. B., and Kepner, R. D.: Meningioma of Thirty Years' Duration: Report of a Case. *Arch. Neur. Psychiat.*, 1943, 50: 327.

This report concerns an enormous meningioma which arose from the dura over the right frontal area and extended down over the hemisphere. The tumor tissue removed weighed 267 gm. The meningioma had previously been operated on in December, 1911, and at that time a piece of tissue was removed from the orbital surface of the roof of the orbit at which point it was firmly attached to the bone.

The second operation was performed in December, 1939, at which time the tumor was removed in its entirety with the overlying dura mater to which it was firmly attached. The dural defect was repaired with fascia lata, and after a somewhat stormy convalescence which was complicated by a stiff neck, cloudy spinal fluid, a sudden and unexplained hemorrhage of bright blood from the rectum about two weeks after the operation, and an attack of jaundice which appeared six weeks after the operation, the patient finally recovered. For a time he showed considerable improvement in his behavior, which had been erratic, but he finally lapsed back into excessive drinking and had to be confined to an institution. ADRIEN VERBRUGGHEN, M.D.

SPINAL CORD AND ITS COVERINGS

List, C. F.: Multiple Meningiomas: Removal of Four Tumors from Region of the Foramen Magnum and Upper Cervical Region of the Cord. *Arch. Neur. Psychiat.*, 1943, 50: 335.

Multiple meningiomas may occur in any part of the nervous system, and this case concerns a group of meningiomas situated at and around the foramen magnum. The patient had complained of headaches in the occipital region for over two years and had developed a progressive weakness in the arms and legs until she became practically paralyzed. Sensory disturbance had not been prominent. There were rigidity of the neck, nystagmus with spastic paresis of all four limbs associated with mild ataxia, hyperactive deep reflexes and abolished superficial reflexes, and a sensory level about the level of the fourth thoracic dermatome. There was no limitation of movement in the diaphragm, and the roentgenograms of the cervical spine were regarded as normal. Lumbar puncture showed a partial block with 182 mm. of total protein.

About nine months later the patient returned for operation, at which time four distinct small meningiomas were seen and removed from the region just above and just below the foramen magnum. The patient made a satisfactory recovery, and after her

operation was able to perform household duties without difficulty.

The article is well illustrated and should be instructive to those interested in neurological surgery.

ADRIEN VERBRUGGHEN, M.D.

Hyndman, O. R., and Wolkin, J.: Anterior Chordotomy: Further Observations on Physiological Results and Optimum Manner of Performance. *Arch. Neur. Psychiat.*, Chic., 1943, 50: 129.

This report consists of an analysis of further studies on chordotomy, with particular reference to the physiology of the anterior and anterolateral columns and to deductions concerning the location and manner of performance of chordotomy for optimum results. Studies of the influence of anterior chordotomy on various types of sensation show that the sense of tickle (that sensation produced by lightly scratching the sole of the foot) remains unaltered after section of the spinothalamic tracts. This sensation is associated with the sense of touch and is modified greatly by the "frame of mind." Itch, on the other hand, is a modified form of pain and is abolished by section of the spinothalamic tract. Agents to produce itch must at least penetrate the corneum of the skin. These facts indicate that the endings of pain fibers must be touched to be stimulated, whereas transmitted pressure is adequate to stimulate the endings of touch fibers.

About half of the patients on whom anterior chordotomy is performed experience girdle pain of varying degree. The pain is of a burning, aching character and is usually localized to a narrow band which represents the level of transition from algesia to analgesia. The girdle pain corresponds, not to the segment at which the chordotomy has been done, but to the level of sensory change on the skin. The study indicates that this pain is not due to injury to the sensory roots. The incidence of girdle pain was less frequent when chordotomy was performed at the first dorsal segment than when it was done at the second or third dorsal segments. Adequate sympathectomy has failed to give relief from this pain.

The effect of chordotomy on visceral pain was studied with respect to testicular pain sense and pain in the renal pelvis. In all but 1 of 5 patients who had had bilateral anterior chordotomy, both testicles were painless. Unilateral chordotomy may only partially abolish testicular pain. These results indicate that this type of pain is mediated through the spinothalamic tracts. In a small group of patients, studies on pain in the renal pelvis indicate that a bilateral chordotomy, which results in cutaneous analgesia as high as the fifth dorsal dermatome, will eliminate pain in the renal pelvis caused by forceful distention. If the analgesia reaches only to the seventh dorsal level, the pain is not completely eliminated.

Studies of the influence of anterior chordotomy on the motor system included observations on shivering, on superficial and deep reflexes, and on reenforcement of deep reflexes. Section of the anterolateral column and the greater portion of the anterior column in 3 patients abolished the possibility of shivering below the section. Shivering appears to be an ipsilateral phenomenon.

Qualitative studies revealed no significant change in the activity of the abdominal and cremasteric reflexes after anterior chordotomy. Section of the anterior half of the cord results, at most, in transient flaccid paralysis and a longer-lasting loss of extensor tone or sustained antigravity reflex. The descending extrapyramidal tracts are not indispensable to normal strength and movement patterns in man, although the tracts in the anterior column appear to contribute to the sustained contraction of the antigravity muscles. When the anterior half of the cord was divided, signs of upper motor-neuron involvement did not appear. It is assumed that in the performance of this type of chordotomy, at least in some patients, the pyramidal tracts were injured sufficiently to have resulted in upper motor-neuron signs had the neural mechanism necessary for their development not been interrupted. Anterior chordotomy did not appear to abolish the effect of re-enforcement on deep reflexes in 3 patients.

The influence of anterior chordotomy on potency and sexual physiology could be deduced from the results in 9 patients. The bilateral procedure is almost certain to abolish erection and orgasm in the male, and orgasm in the female. The desire for intercourse is not lost. It appeared that the tracts subserving the function of psychologically controlled erection and the sensation of orgasm were probably located close to the gray matter in the anterolateral column. The sensation of orgasm is probably a specialized sensation and not a modality of pain or temperature, or of touch sense. Bowel and bladder function are much less impaired, often only transiently. Menstruation has not been impaired after any type of anterior chordotomy. One patient became pregnant and delivered a normal child, with a normal labor mechanism except for absence of pain during the first stage of labor.

Anterior chordotomy did not influence thermoregulatory sweating and had little influence on the known arteriolar reactions, as indicated by the capillary flushing and reflex vasodilatation from heating of the body. There was relatively little alteration in the reaction of the blood pressure to the cold pressor test and to glyceryl trinitrate. The average blood pressures were reduced considerably for from three to six months. Anterior chordotomy at the first dorsal segment, combined with section of Lissauer's tract, ordinarily brings the level of analgesia to the first dorsal dermatome and is useful in abolishing pain high in the chest. JOHN L. LINDQUIST, M.D.

SYMPATHETIC NERVES

De Takáts, G.: Nature of Painful Vasodilatation in Causalgic States. *Arch. Neur. Psychiat.*, 1943, 50: 318.

Causalgia has been of great interest to surgeons ever since its frequent occurrence in the war in 1913.

It has, hitherto, been regarded as an isolated clinical entity, but the author believes that it is allied to those clinical conditions such as Sudeck's atrophy and Leriche's post-traumatic painful osteoporosis. Other clinical manifestations probably belong in this field, as, for instance, the chronic traumatic edema. Hitherto, many of these states have been regarded as possible compensation neuroses, even malingering, and this discussion is, therefore, a timely one.

There are three stages of this syndrome. With the first stage, the traumatized limb is subject to severe and persistent pain of a burning character with paroxysmal exacerbations; in fact, this stage resembles an early dystrophy. The extremity is now warm and dry, and studies of the blood flow show an increased circulation to the injured part. The syndrome may cease to develop at this point, or it may progress further to the second stage. In this stage the part is not warm as heretofore, and may seem hard, cyanotic, and cold. An early atrophy of bone may make its appearance. There is still evidence of vasodilatation in the limb; the blood flow is not active in this stage. In the last stage the atrophy has progressed to involve the skin, muscle, and bone, and the osteoporosis is not distinguishable from that due to inactivity or senility. The patient may have become so affected by persistent pain that, frequently, suicide or commitment to an insane asylum ends the history. At this stage, even radical operative procedure for the relief of pain, such as cordotomy, may be unavailing.

The article goes on to give examples of cases studied, with records of the blood flow and the mechanism of the disturbance. This is, as yet, by no means clear, but cholinergic vasodilator fibers have been implicated. The treatment consists of diagnostic sympathetic blocks of appropriate nerves followed, if necessary, by operative sympathectomy. Early recognition of the syndrome with early and repeated sympathetic block is of utmost importance.

In all, 36 cases were studied in which the phenomena of spreading neuralgia and spreading vasodilatation were seen. In many of them the injury was slight as compared with the trouble which followed.

ADRIEN VERBRUGGHEN, M.D.

Schwartz, H. G., and Findley, T.: Preliminary Observations Concerning Paravertebral Injection of the Sympathetic System in Hypertension. *Surgery*, 1943, 14: 267.

Although the surgical therapeusis of hypertension by sympathectomy is a very valuable procedure, its usefulness could be greatly enhanced by a means of preoperatively determining which patients will have good results. The authors suggest that this may be done by bilateral paravertebral alcoholic blocks to correlate roughly the combined areas denervated by the operations of Peet and Adson.

The technique consists of inserting spinal needles about three fingerbreadths lateral to the spinous processes down to the transverse processes; the needles are then angled downward and medially at an angle of 20 to 30 degrees to a depth of from 3 to 3.5 cm. beyond the rib articulation level to rest against anterolateral surface of the vertebral bodies. Precautions are taken to make sure the needles are not in the pleural cavity or intervertebral foramina. Two cubic centimeters of 1 per cent procaine hydrochloric acid are injected, followed by 3 or 4 cc. of 80 per cent alcohol. The areas of injection are the 10th, 11th, and 12th thoracic segments, the 1st lumbar segment, and the splanchnic nerves. Verification of injection is made by testing the skin sweating.

In 3 cases thus injected there was a striking improvement which lasted for six months, at which time the sweating test revealed that the effects of the injection had worn off in 2 cases. The third case had a recurrence of the former symptoms in about one month. In all of the cases there was a drop of blood pressure for about twenty-four hours.

The lack of correlation of the arterial tension to the subjective improvement after sympathectomy, as shown by Peet, Adson, and Smithwick, has also been observed.

JACK I. WOOLF, M.D.

SURGERY OF THE THORAX

TRACHEA, LUNGS, AND PLEURA

Homans, J.: Pulmonary Embolism Due to Quiet Venous Thromboses and Simulating Cardiac and Pulmonary Disease. *N. England J. M.*, 1943, 229: 309.

Postoperative pulmonary embolism has been frequently recognized and has received considerable attention. Pulmonary embolism without operation or trauma, called silent embolism, may also occur, and in seemingly well individuals. This latter type of embolism is more apt to cause rapid pulmonary infarction without fatality than that which complicates operations, accidents, or an illness.

From a study of the post-mortem findings at the Massachusetts General Hospital, Boston, it was found that 70 per cent of the cases of medical pulmonary embolism harbored phlebitis that gave no evidence of its presence. The author stresses the fact that pulmonary infarction should be strongly considered in the differential diagnosis of pulmonary disease in ambulatory patients since about one-third of the cases of pulmonary infarction occur in patients who have had no operation, accident, or demonstrable cardiac disease.

The condition under discussion is a noninflammatory reactionless process which takes place in the deep veins of the legs. Since the process is silent, the danger of embolism is greater. Recovery from the condition may take place without operation, although 3 of the 5 patients treated by the author failed to recover. The development of femoroiliac thrombophlebitis is seldom observed. The formation of a propagating thrombosis with pulmonary embolism was seen in 11 cases which were reported in some detail by the author. Nine of the 11 were in men. Their ages varied from twenty-eight to sixty-three years. Multiple embolism occurred 6 times. In addition to the 11 idiopathic cases there were 6 others in which an old thrombophlebitis, an injury, or illness preceded the thrombosis.

Treatment by division of the vein was carried out in 10 patients. The level of division was thought best to be in the common iliac vein since this would allow for collateral circulation better than division of the common femoral vein. Recovery with good results followed operation in 9 of 10 patients. The case which was not treated surgically terminated fatally. WILLIAM E. ADAMS, M.D.

Rafferty, T. N.: Artificial Pneumothorax. *J. Thorac. Surg.*, 1943, 12: 578.

Continued failure to establish and emphasize adequate standards for artificial pneumothorax has constituted a fundamental defect of collapse therapy. Improved perspective now makes it clear that pneumothorax may act in widely different ways and that, as with most surgical procedures, therapeutic results are favorable only in proportion to the care exhibited in their use and to the faithfulness with which basic, objective principles are carried out by the surgeon.

The basic aims of management are the reduction of complications to an absolute minimum, and the differentiation, as early as possible, between an effective and ineffective pneumothorax. Neither of these is attainable unless surgical aid is readily available; in addition, pneumothorax must be conceived as only part of the collapse-therapy program.

The author outlines the major points in his experience which contribute a more rational understanding of pneumothorax. Some of these factors are the result of recent technical developments; most of them, however, merely represent the application of ordinary sound surgical principles. It seems probable that the widely divergent opinions as to the value of pneumothorax are mainly a reflection of the many illogical ways it has been used. When the present loose conception of it is corrected and it comes to be used in such a way that the term pneumothorax automatically connotes an effective well managed procedure, the controversy over its merit will largely disappear.

The application of collapse therapy along these general lines will result in a moderate percentage decrease in the use of artificial pneumothorax and a moderate to marked percentage increase in the use of thoracoplasty. CHARLES BARON, M.D.

Ceballos, A.: An Operation Performed in One Stage With Inhalation Anesthesia for Hydatid Cysts of the Lung, Free of Adhesions. *J. Thorac. Surg.*, 1943, 12: 553.

The author reports on 24 patients who were operated upon under inhalation anesthesia. All of these patients had hydatid cysts of the lung with a free pleura and in all cases there existed the danger of infection of the pleura. The object of the inhalation anesthesia was to counteract the pneumothorax that necessarily takes place when the pleura is incised, and also to keep the lung in which the cyst is localized in contact with the operative incision. The production of an operative pneumothorax is not always a grave complication even though in some cases simultaneous complications have occurred.

The method most commonly used to avoid operative pneumothorax was Posadas' method, that is, suturing the lung to the chest wall and emptying and closing the cyst. With inhalation anesthesia this maneuver is avoided. The cyst can be evacuated easily, and the cavity can be marsupialized and closed. This is of great advantage. It does not leave a residual pneumothorax and the distended lung later occupies the pleural cavity in the same way that it normally does. Only 1 death occurred

because of a pulmonary abscess and bronchial pneumonia. One patient developed a purulent effusion in the pleural cavity, but it was not necessary to drain this. Later 4 cases of nonpurulent pleural effusions that disappeared spontaneously were seen. During the execution of the operation no complications were observed which might worry the surgeon. No suffocation, hemorrhage, or emphysema have been noted as the result of hyperpressure anesthesia. Patients with multiple hydatid cysts who have been operated upon in different stages have tolerated the anesthesia with hyperpressure without effect on the other cysts existing in the lung. To effect hyperpressure it is necessary to use intratracheal intubation. If this is not used, the gas administered at a pressure of 15, 18, or 20 mgm. of mercury may pass through the pharynx and produce distention of the stomach. Hyperpressure through the simple facial mask does not distend the lung so completely as when the administration is carried out through a tracheal tube. Hyperpressure administered in cases of hydatid cysts of the lung presents some problems not encountered in other pulmonary diseases at the time of operation, because the cyst is filled with liquid and is subject to the changes of increased bronchial pressure. It is necessary, therefore, to graduate the hyperpressure and use it with caution.

The first and most fundamental thing is the exact localization of the cyst. This must be done by the surgeon himself by means of fluoroscopy and roentgenography. The patient should be placed in the same position in which he is to be operated upon because change in position may cause a shift in the position of the cyst. The preparation of the patient has no unusual features and involves only those common to all major operations.

The existence or nonexistence of pleural adhesions cannot be affirmed in a categorical way before the operation. It can only be presumed through the change in the cyst's shape and the history of the pleural pain that pleural symphysis may be present. The presence of adhesions can be established only by preoperative pneumothorax, but this is of no importance in the technique. There are some cases in which it is possible to determine definitely the existence of pleural symphysis. In these cases, the use of intratracheal inhalation anesthesia is not necessary. In the instances in which adhesions are suspected, it is not necessary to investigate with more or less complicated methods.

When the cyst has been localized and the patient placed in the position for operation, the anesthetic is administered, first with a simple mask; then, when the patient is asleep, a tube is placed in the trachea by way of the nose. If there are, however, certain obstacles caused by deviations in the anatomy of the nose, or any other reasons, the tube may be introduced through the mouth. The intubation is usually done when the patient is asleep, but sometimes it is done when the patient is awake, following local anesthesia to the pharynx.

When the cyst is localized, a rib is resected over the cyst. As a rule, the cysts of the superior lobes are approached anteriorly, the lesions of the middle lung fields through the lateral chest wall, and those of the lower lobes through the posterior chest wall. For cysts of ordinary size, the resection of one rib is usually enough, but when the cysts are small and more difficult to localize, it is usually more convenient to resect two ribs. After the ribs are resected, the pleura is opened, and at that moment the anesthetist, to diminish the intrapulmonic pressure, permits a slight pneumothorax. If the cyst is not palpable and visible through the visceral pleura, this maneuver may aid in localization. Once the precise localization of the cyst is established the lung is again distended and there is usually no need to surpass 18 mm. of mercury in pressure. The cyst is then punctured with a Finochetto aspirator and a medium-sized trocar, and the aspiration of the liquid in the cysts is begun. This liquid is quickly evacuated together with the germinative membranes or the daughter vesicles when they exist. The lung is kept inflated and if there are any bronchi of sufficient caliber to affect the intrapleural pressure which open into the cyst, it is convenient to increase the intrabronchial pressure. The cavity is then plugged with gauze, marsupialized, and closed. This plan is practical for all simple cases in which the cyst is peripheral or in contact with the thoracic wall. There are sometimes difficulties in the marsupialization of "central cysts," in which there is a portion of parenchyma between the cyst and the chest wall. When the cysts are small there is a tendency to close the wound without drainage. The trocar aspirator can be used in much the same manner as a harpoon; it favors the traction of the lung toward the operative opening, even when the increase of intrabronchial pressure has a tendency to fix the lung. Cysts localized in the vicinity of the pulmonary hilum, with a considerable amount of parenchyma covering them, may be dealt with in this manner.

The advantages of this method are that it considerably shortens the postoperative period, in comparison to the two-stage procedure, and that it facilitates the operation more than the "harpooning method," which always presents some difficulty. It also favors the evacuation of the cyst. The author has not observed bronchial overflow, suffocation, hemorrhage or effusion, or spilling of liquid or of daughter vesicles into the pleural cavity in any case. The most outstanding advantage of the method is that all of the maneuvers necessary for the cure of the patient are performed in one operation.

This method has resulted in a 4.16 per cent mortality in cases of cysts free from adhesions. The risk is somewhat greater in adherent cysts, although in almost all of the adherent cases there were secondary infections or other infectious complications. It is necessary to stress again the importance of precise localization of the cyst, so that unnecessary

aspirations will not be made because of miscalculation in the localization. CHARLES BARON, M.D.

Tyson, M. D.: The Surgical Management of Solitary Cysts, or Cystlike Structures, of Pulmonary Origin. *Ann. Surg.*, 1943, 118: 50.

Cystlike structures of the lung may be congenital or acquired. The author in a review of the literature was able to find approximately 400 cases and reported 7 additional personal cases.

Most of these cysts present themselves for treatment because of some accident to the cyst, such as infection, or alteration of the mechanical air exchange through a connecting bronchus. Of the 7 personal cases reported, 6 were operated upon successfully, the seventh case being asymptomatic. Of the various accidents that may occur to the cyst, the following were demonstrated by the author's patients: (1) infection of the cyst, (2) rupture of the cyst with sterile fluid in the pleural cavity, (3) infection of the cyst with pyopneumothorax, (4) infection of the cyst and mechanical difficulties with bronchial air exchange, (5) spontaneous pneumothorax, and (6) tension pneumothorax.

Frequently the true nature of the cyst or cystlike structure is overlooked and the complications such as empyema and lung abscess are mistaken for the primary pathology. In only 3 of the 7 cases was a positive diagnosis of cyst made when the case was first seen.

Of the 6 cases operated upon, 4 were congenital cysts of pulmonary origin. Two of these were cystic accessory lobes arising outside of the normal lung tissue. Two of the 6 probably represented an emphysematous bulla instead of a true pulmonary cyst. However, they are included in this report since the manifestations were not unlike those of a true pulmonary cyst. WILLIAM E. ADAMS, M.D

Blades, B.: Conservation of Lung Tissue by Partial Lobectomy. *Ann. Surg.*, 1943, 118: 353.

Until recent times pulmonary resections, in the majority of cases, have been accomplished as rapidly as possible by mass ligation of the hilum of the lobe in order to shorten the operative time. With improvements in anesthetic techniques and other surgical measures, more deliberate operative procedures are possible. In earlier years the conservation of lung tissue was accomplished by the removal of only the lingula of the left upper lobe, as has been brought out by Churchill and his associates. This principle may be applied to other parts of the lung and is especially applicable in the treatment of bronchiectasis.

The lower lobe may be divided into the dorsal and basal divisions, and the latter may be subdivided into the anterolateral segment, anteromedial segment, posteromedial segment, and posterolateral segment. The dorsal portion of the lower lobe is not infrequently separated from the basal portion by a definite fissure and may be managed very easily as a separate unit. A case is reported by the author in which this portion of the lower lobe contained a pulmonary abscess and was removed without disturbance of the remainder of the lobe. He stated that this is the most common site of pulmonary abscess in the lower lobe. Resection of portions of the basal division of the lower lobe is less frequently indicated. It may be accomplished by the use of a clamp and division of the lung tissue distally, with identification of segmental branches of the air passages and blood vessels.

The middle lobe is rather small and rarely lends itself to partial removal. However, the left middle lobe, or the lingula of the left upper lobe, is commonly removed since involvement of this portion of the upper lobe by bronchiectasis is present in over 60 per cent of the cases presenting involvement of the left lower lobe.

The upper lobe may be divided into anterosuperior, posterosuperior, anterolateral, and anteroinferior segments. Only occasionally may a portion of this lobe be removed and the remainder spared, for instance, when the lower and middle lobes have been removed for bronchiectasis and the disease involves also the anteroinferior or lateral segments of the upper lobe.

Occasionally a definite diagnosis cannot be made from gross palpation of a pulmonary lesion. By performing a partial lobectomy and further examining the lesion after removal of the mass, the surgeon may avoid radical surgery when it is not indicated. The author reports the case of a patient in the armed forces who underwent lingualectomy and partial left lower lobectomy for bronchiectasis, after which he returned to active duty.

One suggestion regarding technique was offered: that parietal pleura obtained from the chest wall be used to cover the raw surface which remains following a partial lobectomy.

WILLIAM E. ADAMS, M.D.

HEART AND PERICARDIUM

Blalock, A., and Ravitch, M. M.: A Consideration of the Nonoperative Treatment of Cardiac Tamponade Resulting from Wounds of the Heart. *Surgery*, 1943, 14: 157.

It is now generally agreed that wounds of the heart, especially of the ventricles, with resulting tamponade should be treated by operation, i.e., pericardiotomy with suture of the wound. In wounds of the auricles and possibly of the right ventricle, however, a conservative form of treatment must be considered. Simple aspiration of the pericardial cavity may be successful in some cases, while in others it may temporarily improve the condition of the patient and give time for an eventual operative intervention. While it is a definite hazard not to operate on a patient with a stab wound of the heart, on the other hand it must be considered that the mortality rate from wounds of the heart which have been treated by operation is at least 50 per cent. The question arises as to whether conservative

treatment in selected cases could reduce the mortality rate.

In the 4 instances reported in this paper the patient's condition improved following pericardial aspiration; in 1 case the aspiration of only 30 cc. of blood from the pericardial sac followed by blood transfusion produced a dramatic response. Only 1 patient underwent a successive open operation which, from the type of wound found in the heart, appeared to be unnecesssary. It is evident that if blood reaccumulates rapidly within the pericardium after aspiration, exposure and suture of the heart wound should not be further deferred.

In conclusion the authors agree with the directions prepared recently for medical officers in the U. S. Army. These directions are as follows:

1. Aspirate the blood from the pericardium by means of the costoxiphoid route, if possible.
2. Repeat if there is a recurrence.
3. If a second recurrence takes place, perform a cardiorrhaphy through an extrapleural exposure.

CONRAD L. PIRANI, M.D.

ESOPHAGUS AND MEDIASTINUM

Cleaver, E. E.: Chronic Peptic Ulceration of the Esophagus. *Am. J. Digest. Dis.*, 1943, 10: 319.

Peptic ulceration of the esophagus was found by the authors not to be a rare disease. To substantiate this statement 10 personal cases were reported. The symptoms associated with this condition were usually pain, hematemesis, and dysphasia. The lesion was usually situated in the lower third of the esophagus and occurred not infrequently in patients with a congenitally short esophagus, with diaphragmatic hernia, and with a part of the stomach in the chest.

The pain was usually in the region of the epigastrium and at times radiated forward and around to the back. Hemorrhage was rapidly fatal because of erosion of the aorta; however, it was usually less severe. Dysphasia was mild or severe and swallowing finally became impossible.

Two complications were commonly seen: (1) perforation of the ulcer into the pleura, pericardium, or bronchus, and (2) acute mediastinitis due to spread of infection from the ulcer into the surrounding tissues. The diagnosis was usually based on the symptoms and x-ray findings on swallowing barium.

Treatment may be the same as for gastric or duodenal ulcer. However, when a congenitally short esophagus and diaphragmatic hernia are present this may not be effective. Tincture of belladonna has been found to be of some value. Feeding with a duodenal tube is useful. Operation was not advised in any of the cases. WILLIAM E. ADAMS, M.D.

Ravitch, M. M.: Suppurative Anterior Mediastinitis in an Infant Following Intrasternal Blood Transfusion; Operation and Recovery. *Arch. Surg.*, 1943, 47: 250.

The author prefaces his report with a rather extensive account of the history of intramedullary therapy. This is especially noteworthy because in the case reported an intramedullary transfusion was attempted with serious consequences. The first records of marrow puncture go back as far as 1903. In 1928 and 1929 sternal puncture became a highly popular diagnostic method among hematologists, particularly abroad. In the years that followed a vast amount of experimental work was being carried out which was concerned with intramedullary injections of every conceivable substance. The present interest in the intrasternal and other intramedullary routes for the administration of blood and fluids was aroused by the recent publications of Tocantins and O'Neill on the infusion of blood and other fluids into the general circulation via the bone marrow (1941).

Intravenous therapy of all sorts, particularly the administration of fluids, blood, and plasma, has come to play such a large part in present-day therapeutics that the number, size, and durability of a patient's veins may actually represent the difference between easy and adequate treatment on the one hand and difficult and inadequate treatment on the other. This observation is especially applicable in a long illness. For this reason the suggestion that the marrow spaces of the sternum, femur, and tibia be used for intravenous infusions, seemed to present a solution to the problem of administration of fluids to patients "without veins."

The author takes the stand that the number of adult patients a year who finally reach the point at which intravenous medication is all but impossible is extremely small and that even for these it is usually possible to have recourse to the jugular and the femoral veins to give enough fluid for several days until the more frequently employed superficial veins are once more usable as a consequence of resorption of extravasations, canalization of old thrombi, or enlargement of collateral vessels. In the case of infants, superficial veins always seem to be available.

Despite the apparent advantages of a method which requires one to strike only the marrow cavity of a bone instead of the lumen of a fragile vein, the infusion of fluids into the bone marrow is an unnecessarily hazardous procedure. This method not only is trying for the patient, but on the basis of the figures supplied by the proponents of the method, it will not deliver quantities of fluid with sufficient rapidity to justify its use. The method requires special skill and experience, which are to be gained only from constant use, but its use without its special indications, which exist only in occasional cases, is not justifiable.

Most discussions of mediastinitis deal with infections of the posterior mediastinum. Posterior mediastinitis results from esophageal or tracheal perforation, disease of the tracheobronchial lymph nodes, diseases of the lungs or of the pleura, and extensions from cervical infections. The anterior mediastinum rarely becomes involved by cervical and posterior mediastinal infections. In consequence anterior mediastinitis is an uncommon condition. A number of anterior mediastinal abscesses following simple fracture of the sternum have been described

in the literature. Acute hematogenous osteomyelitis of the sternum may cause acute suppurative anterior mediastinitis.

The most important specific symptoms of acute suppurative anterior mediastinitis are edema of the head and arms with venous distention in the same region, and dyspnea. There is also usually acute hypertension. All authors agree on the necessity of early resection of portions of the ribs or sternum, or both.

The present article reports a case of suppurative anterior mediastinitis in an infant of eight months following attempted intrasternal transfusion of blood through a needle inserted for the purpose of making a sternal puncture. The blood had been drawn six days previously and had been used two days before for an intravenous transfusion in the same child. The case came to the author's attention when surgical consultation at the Harriet Lane Home of the Johns Hopkins Hospital, Baltimore, became necessary because of serious complications which followed this intramedullary transfusion, which had been attempted at another hospital. After the infant was transferred to the Harriet Lane Home she was edematous and almost moribund, yet no difficulty was encountered in giving blood and fluids at will by percutaneous puncture through veins of the scalp and the extremities. Fever, dyspnea, edema of the face and arms, and broadening of the mediastinal shadow were present. The head was held retracted and there was hypertension. Fluoroscopic examination showed a mass in the anterior mediastinum, overlying chiefly the base of the right ventricle.

There was general agreement that the patient presented the picture of obstruction to the superior vena cava due to the introduction of blood into the anterior mediastinum, where under the fluoroscope a mass could be plainly seen. It was thought that the moderate hypoproteinemia which was present permitted the rapid appearance of edema.

There was some dispute as to whether there was merely a collection of blood, which could be trusted to resorb in time, or an actual abscess. Aspiration in the third interspace parasternally, which was the area of maximal dullness to percussion, yielded reddish brown pus. Recovery followed resection of the overlying sternum and costal cartilage with drainage of the abscess and of the diffuse mediastinitis.

In the present instance, since there was nothing in the history of the case to indicate that the child had an infection of the blood stream before or after transfusion, the appearance of pus in the mediastinal extravasation suggests that the blood may have been contaminated. A few organisms introduced into a vein, and probably into the bone marrow, are ordinarily of no consequence. In the mediastinum the results can be extremely serious.

MATHIAS J. SEIFERT, M.D.

Adams, W. E., and Thornton, T. F.: Bronchogenic Cysts of the Mediastinum. *J. Thorac. Surg.*, 1943, 12: 503.

Bronchogenic cysts of the mediastinum have been infrequently reported. In the readily available literature less than 50 cases were found. The authors report 3 cases illustrating several of the commoner characteristics of this lesion.

Although the origin of these cysts is not well understood, in all probability it is similar to that of cysts occurring within the pulmonary tissue. Most bronchogenic cysts are located on the right side just above the carina; they are thin-walled, filled with a thin mucoid material containing desquamated epithelium, and lined with low cuboidal or columnar epithelium. The wall of the cysts consists of fibrous tissue, muscle, and mucous glands, and it usually contains some cartilage, nerves, and blood vessels. The symptomatology depends upon the size and location of the cysts and whether pressure interferes with adjacent structures. Many cysts produce no symptoms and are found accidentally. Others, by pressure on the trachea or bronchi, may produce anoxia or infection of the respiratory passages.

Two of the 3 reported cysts were asymptomatic. The third, because of its communication with the left primary bronchus, produced a picture similar to that of pulmonary suppuration. All 3 patients underwent either partial or complete removal of the cyst wall and were asymptomatic following the operation.

SURGERY OF THE ABDOMEN

GASTROINTESTINAL TRACT

Rekers, P. E., Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Cancer of the Gastrointestinal Tract. *J. Am. M. Ass.*, 1943, 122: 1243.

The authors report observations on pancreatic insufficiency in a patient who had had the duodenum and head of the pancreas resected and the pancreatic ducts ligated for carcinoma of the ampulla of Vater.

On a measured diet the patient was found to excrete excessive amounts of fat and nitrogen in the feces as compared with control subjects. The excess of nitrogen excreted in the feces was demonstrated to be of dietary origin. The possible causes for this functional disorder were considered to be (a) an inability to digest fat and nitrogen into those compounds which could be absorbed, (b) an inability to absorb even simple fat and nitrogen compounds, or (c) an excessive intestinal secretion of fat and nitrogen compounds.

The oral administration of amino acids did not increase the nitrogen excretion, but a diminished nitrogen intake rapidly diminished the amount in the feces. Hence, it was concluded that the digestion of protein was impaired and not the absorption of the end products of protein breakdown.

The administration of bile salts and lipocaic had no effect, but the administration of external pancreatic enzymes in the form of pancreatin was followed by a prompt decrease in the excessive fat and nitrogen output in the feces and a reduction in the frequency, bulk, and foul odor of the stools.

During the course of this study it was also observed that an increase in the protein content of the diet resulted in increased absorption of fat, and an increase of the fat content of the diet resulted in an increase in the amount of fat absorbed but no decrease in the amount of fat excreted.

EDWARD W. GIBBS, M.D.

Guyer, R. B.: The Comparison of Radiological and Gastroscopic Findings in 200 Dyspeptic Soldiers. *Brit. J. Radiol.*, 1943, 16: 241.

In 1942 the authors analyzed the "dyspeptic soldier" by examining a series of 200 cases, both radiologically with an opaque meal, and gastroscopically. The soldiers were between the ages of nineteen and forty-eight years. Preliminary fractional test meals and occult-blood stool examinations completed the studies.

The combined radiological and gastroscopic findings are shown in Table I.

TABLE I.—RADIOLOGICAL AND GASTROSCOPIC ANALYSIS OF CASES

Radiological findings	Gastroscopic findings	No. of cases	Percentage of cases
Normal	Normal	78	39.5
Normal	Gastritis	61	30.5
Normal	Healing gastric ulcer	7	3.5
Normal	Sessile adenoma	1	0.5
Duodenal ulcer	Normal	10	5.0
Duodenal ulcer	Gastritis	7	3.5
Duodenitis	Normal	1	0.5
Duodenitis	Gastritis	13	6.5
Gastric ulcer	Gastric ulcer	7	3.5
Gastric delay	Gastritis	2	1.0
Gastric delay	Normal	4	2.0
Gastritis	Gastritis	5	2.5
Gastric spasm	Healed gastric ulcer	2	1.0
Duodenal diverticulum	Normal	1	0.5

One may note that there is a considerable discrepancy between the two types of examinations, especially in the cases showing gastritis. This is easily explainable. The radiological examination gives information concerning the coarser anatomical details of the stomach, whereas gastroscopy permits a closer viewing of the finer details of the mucous membrane. Thus, in a complaint of dyspeptic nature, radiology often fails to elicit any cause of disorder and the findings apparently are normal. Gastroscopy, however, reveals mucosal changes, such as patchy hyperemia, edema, hemorrhages, or (during the process of healing) areas of brown pigmentation, all of which indicate not only the presence, but also the degree or type of gastritis. In a series of 61 cases the gastritis was found to be mild—superficial in 18 cases, severe active-superficial in 28, atrophic in 12, and hypertrophic in 3.

In 2 other lesions the combination of radiology and gastroscopy offered considerable scope: (1) cases of healed or healing gastric ulcer which had passed beyond the stage of radiological visualization, and (2) cases of very early malignant change in which the lesion was as yet too small to be detected radiologically.

In the study of the duodenum, radiology stands supreme. Gastroscopy allows only the corroboration of secondary changes which may be present in the gastric mucosa.

The final conclusion is reached that the two methods of investigation are complementary to each other. In patients constantly reporting sick with dyspeptic symptoms, when all other forms of examination have remained negative, gastroscopy is of greater assistance inasmuch as it permits the diagnosis of gastritis and thus facilitates the treatment or disposal.

T. LEUCUTIA, M.D.

Fowler, R. H.: External Trauma and Peptic Ulcer. *Indust. Med.*, 1943, 12: 614.

The author places the incidence of primary peptic ulcer resulting from a single blunt traumatism at 0.6 per cent. To establish the authenticity of traumatic ulcer, four postulates must be fulfilled:

1. Proof of absence of previous subjective gastric complaints
2. Proof of authenticity of the trauma
3. The external injury must be a direct, blunt force of sufficient severity to cause the lesion
4. Symptoms referable to the stomach must be immediate and merge with those of ulcer, and permit a diagnosis by x-ray study, operation, or autopsy examination.

The author also presents the medicolegal aspects of these lesions and cites at length 9 litigated cases.

J. M. MORA, M.D.

Westhues, H.: Development of Stomach Cancer From Gastritis and Inflammatory Polyps? (Entstehung des Magencarcinoms aus Gastritis und entzuendlichen Polypen?) *Arch. klin. Chir.*, 1942, 203: 391.

According to the author's opinion, gastritis is of no paramount importance in the genesis of gastric cancer. An inflammation is no causative factor in the development of blastomatous gastric polyps, of which a precancerous character is not denied but emphasized. The author does not deny the possibility of a development of carcinoma from gastritis, but, contrary to Konjetzny's views, he does not believe that such occurrence is frequent. Konjetzny maintains that gastritis is responsible for 85 per cent of all gastric carcinomas. If this were the case, energetic prophylactic treatment in the form of a resection would be required in each case of gastritis, particularly in view of the fact that not less than 6 per cent of all men over twenty years of age die from gastric cancer, from 40 to 50 per cent of all cancers being located in the stomach. Konjetzny himself is very moderate in his demands for preventive resection in patients with gastritis. His conservatism in this respect is not in accord with his theoretical consideration. According to the view of the author of this article, only the gravity of the symptoms of gastritis should bear influence on the decision whether a resection should be performed or not.

An increased frequency of gastritis in recent years did not contribute to the rise of frequency of gastric carcinoma.

In contrast to hyperplastic proliferations of the mucosa of inflammatory character, blastomatous polyps are frequently solitary. If such polyps were of an inflammatory origin, it would be difficult to explain why a gastritis should lead to a formation of an isolated, single polyp. Moreover, purely inflammatory proliferations in the form of a hyperplasia are usually absent in the immediate vicinity of blastomatous solitary polyps. A more marked inflammation in the form of a chronic gastritis cannot be found in the majority of cases in which single polyps are present. An inflammation may be the result but not the cause of a polyp. Conversely, blastomatous polyps are not found with increased frequency in cases with a diffuse, chronic gastritis. On the other hand, chronic, inflammatory processes accompanying a callous ulcer, not infrequently lead to the formation of a marginal cancer. It may be concluded that neither blastomatous polyps nor cancers originating from them are of an inflammatory character.

JOSEPH K. NARAT, M.D.

Mulsow, F. W.: The Low Incidence of Cancer of the Stomach in Iowa. *Am. J. Digest. Dis.*, 1943, 10: 297.

So few cases of cancer of the stomach had been seen in Iowa over a period of years that a study of the local incidence and diagnosis of gastric cancer was instituted. From this study it appears that many textbooks and writers in medical journals have overestimated the frequency of gastric cancer, or that cancer of the stomach is not as frequent in Iowa as it appears to be in other parts of the United States. All the certified death records for the five years preceding 1935 were examined, but the reliability of the diagnosis seemed so uncertain that the study has started from that date.

Cancer of the stomach has been found to cause about 5 per cent of all cancer deaths in Cedar Rapids during the past eight years, and there were about 5 per cent more patients suspected of having died of gastric cancer. Cancer of the stomach at the Hospital of the State University of Iowa accounts for 5.3 per cent of all cases of cancer admitted there. In a report of the Division of Vital Statistics for the State of Iowa in 1941, it is shown that there were 3,660 deaths from cancer and other malignant tumors. Cancer of the stomach caused 558 deaths, or 15.2 per cent of all deaths from cancer. This is about half the death rate for gastric cancer that many books and periodicals give.

During the past eight years there have been in Cedar Rapids, 734 deaths from cancer and other malignant tumors. There were 91 deaths, or 12 per cent, reported as being due to cancer of the stomach. In many instances the diagnosis was made on very little definite findings. It is well known that gastric cancer is difficult to diagnose. The methods by which the diagnosis was made follow:

Autopsy	10
Biopsy	6
Exploration	17
X-ray examination	13
Clinical findings	18
Doubtful findings	27
Total	91

The low incidence of gastric cancer in Iowa may be affected by the high per cent of rural population, relatively little poverty, more accurate diagnosis in the data presented, and other unknown factors.

A few examples as to how the diagnoses were made may be of interest. Two cases of elderly individuals complaining of gastrointestinal bleeding were recorded as carcinoma of the stomach. Contact with the physician brought the reply that perhaps he made the diagnosis on too little evidence and after more study he now believed that death was probably due to bleeding peptic ulcer. Five cases were reported as cancer of the stomach, when in reality cancer of the abdominal cavity was meant. It is well known that the term "stomach" is often used to cover any condition of the abdomen, especially when there is vomiting. In many other cases the patient refused x-ray examination or hospitalization, or was seen only a few times by the physician, who more or less guessed at the final diagnosis.

STEPHEN A. ZIEMAN, M.D.

Palmer, W. L.: The Duration of Gastric Cancer. *Gastroenterology*, 1943, 1: 723.

The purpose of this article is to call attention to the extremes of growth of gastric cancer, to what might be termed "acute" and "chronic" gastric cancer. Acute carcinoma appears to be featured by the rapidity of the growth and dissemination of the tumors. In 1936 Jarcho described a diffusely infiltrative carcinoma with several varieties of metastases not previously correlated, including the so-called lymphangitic pulmonary metastases and extensive deposits of tumor in the bone marrow leading to severe anemia and thrombocytopenic purpura. The primary tumor was usually gastric in location and infiltrating in type. Palmer reported such a case in 1939 and reviews it. The terminal picture was that of thrombocytopenic purpura and anemia secondary to extensive carcinomatosis following a two and one-half months' course with an initial diagnosis of gastric ulcer. The acute neoplasms tend to be infiltrative and totally undifferentiated histologically.

The duration of symptoms in the average case of gastric cancer coming to the physician for diagnosis is usually from one to two years. The rate of recurrence of growth of the residual cancer following subtotal gastrectomy may be rapid.

The so-called late recurrences of gastric neoplasm after subtotal gastrectomy seem to indicate that certain tumors are characterized by a very slow growth. Cases have been reported with recurrence after eighteen years. A case reported by Eusterman and Balfour is reviewed; in this case a primary gastric carcinoma was resected approximately nine and a half years after the onset of symptoms. Chronic tumors tend to be circumscribed, polypoid, and highly differentiated histologically.

The prognostic significance of the degree of cellular differentiation is emphasized by Walters, Gray, and Priestley, who found that in terms of Broders grading the five-year survival rates after resection were as follows: 86.2 per cent in cases in which the lesions were of grade 1, 58.8 per cent in cases in which the lesions were of grade 3, and 23.3 per cent in cases in which the lesions were of grade 4. The degree of cellular differentiation seems to be the most important single prognostic factor. Unfortunately, the majority of gastric carcinomas belong to groups 3 and 4.

The rate of growth of gastric carcinoma probably depends primarily upon the growth potential of the cell, for which there is no satisfactory measure or criterion except the general knowledge that as a rule the degree of malignancy is inversely proportional to the degree of differentiation. The resistance of the body to cancer is variable. Certainly there are great differences in the amounts of fibrous-tissue proliferation evoked by various tumors.

The therapeutic implication is that, as a rule, all gastric carcinomas should be resected unless the existence of distant metastases is proved. It is possible that in certain cases the removal of the primary tumor may exert a favorable influence upon the growth of the secondary lesions, but at present there is little evidence to support this view.

LEROY J. KLEINSASSER, M.D.

Holloway, J. W.: Regional Ileitis. *Ann. Surg.*, 1943, 118: 329.

Thirteen cases of regional ileitis in its various phases are reported and the attempt is made to outline the possible sequence of events in this disease on the basis of the gross pathological findings in these cases. Many of the observations are confirmatory of previous observations of others. In all of the cases with one exception localization was as Crohn originally described it. Four cases are selected as examples of the various stages of progression and the specimens from these cases are illustrated in color.

The earliest gross manifestations of regional ileitis appear to be marked edema, absence of associated signs of local inflammation, and the presence of peritoneal fluid. This phase is largely a matter of lymphatic block. The second phase is still characterized by lymphatic block with superimposed signs of moderate inflammation. The third phase is illustrated by a specimen showing evidence of lymphatic block with moderate inflammation, characterized by edema, peritoneal fluid, and redness. In this case there was segmental involvement, one area involved being the duodenum, which showed marked edema and a minimal inflammatory reaction. The fourth phase represents the stage of chronicity, fibrotic changes, stenosis, and tumor formation. The first two phases are classified as acute, the third as subacute, and the fourth as chronic. This classification is used in a strictly clinical sense without implications as to microscopic findings.

Differential diagnosis in the acute phase is difficult and if exploration is carried out it is usually undertaken with a diagnosis of acute appendicitis. Roentgenological studies in the acute cases, six to eight weeks after operation, have failed to reveal any findings that were diagnostic. In most instances there had been a complete subsidence of symptoms postoperatively. The friability of the tissues in the

subacute stage might make roentgenography undesirable. Fistula formation and perforation may occur spontaneously in this phase. The chronic forms present much less of a problem from a diagnostic standpoint but require distinction from malignant growths and specific granulomas.

In treatment of the acute stage the author advocates conservatism but removes the appendix when the cecum is uninvolved. Appendectomy is done, not with the idea that it is of therapeutic value, but because absence of the appendix is reassuring should there be a chronic complaint in the right lower quadrant. Because of the friability and tendency to perforation of the intestine the subacute stage may require resection. The chronic stenotic phase is definitely amenable to surgical treatment, with primary resection as choice. JOHN L. LINDQUIST M.D.

Benson, R. E., Dixon, C. F., and Waugh, J. M.: Nonmeckelian Diverticula of the Jejunum and Ileum. *Ann. Surg.*, 1943, 118: 377.

Diverticula occur in the jejunum and ileum which are nonmeckelian in origin. At the Mayo Clinic from 1909 to 1942, inclusive, diverticula of the small intestine, exclusive of duodenal and meckelian diverticula, were observed in 122 cases. In 100 the jejunum was affected. In 17 the diverticula were limited to the ileum and in 5 the diverticula occurred throughout the small intestine. The proximal portion of the jejunum was most frequently affected. These diverticula may occur in any position around the circumference of the bowel; however, the majority are situated along the mesentery. They vary in size from a few millimeters in diameter to large outpouchings. In 44 of the 122 cases only 1 diverticulum was observed. Thirty-seven of these solitary outpouchings occurred in the jejunum and 7 in the ileum.

At the Mayo Clinic most of the diverticula of the small intestine have been found at autopsy (85 cases). Some have been recognized during the course of abdominal operations (21 cases). These diverticula are not easily identified at the operating table. Even when they are distended with intestinal contents, they may offer so little resistance to the palpating hand that they will escape identification. Often they are hidden within the mesentery.

Uncomplicated diverticulosis of the small intestine does not give rise to any characteristic symptoms. Symptoms of chronic intestinal obstruction may be associated with diverticulosis of the small intestine. A remarkable condition is thus produced, and in the cases of this series it was the most commonly observed complication. In this condition the segments of bowel which give origin to the diverticula are markedly dilated and have thick, hypertrophied walls. The changes in the bowel are similar to those found in a loop of intestine which has been obstructed mechanically for a long period.

In 3 of the 6 cases of diverticulosis with symptoms of chronic obstruction of the jejunum in this series, however, the authors did not observe any mechanical obstruction to which could be attributed the dilatation and hypertrophy of the segments of bowel affected by the diverticulosis. This unusual picture of "chronically obstructed appearing" intestine and diverticulosis of the involved segments without demonstrable mechanical interference with the continuity of the bowel may represent a "functional" type of obstruction.

The first reported case of primary carcinoma of a jejunal diverticulum is contained in this article along with several other unique and interesting complications of nonmeckelian diverticula of the jejunum and ileum.

Dockerty, M. B., and Ashburn, F. S.: Carcinoid Tumors (So-Called) of the Ileum: Report of 13 Cases in Which There Was Metastasis. *Arch. Surg.*, 1943, 47: 221.

In a review of the records and pathological specimens of 130 carcinomas of the small intestine, 30 so-called carcinoid tumors were encountered. Thirteen of these had metastasized locally or distantly. These 13 tumors affected persons in the older age groups and in 9 instances were responsible for disabling symptoms, chief among which were those indicative of chronic intestinal obstruction.

Preoperative diagnosis of the type of lesion was not possible, but radical surgical procedures were carried out in the majority of cases, with results in accord with results which had followed similar procedures used in dealing with carcinoid tumors. Fresh tissue identification of type was of considerable assistance in deciding this issue of treatments. Follow-up studies appeared to justify the type of treatment employed.

Pathologically the neoplasms tended to be present in the terminal segments of the ileum as small orange submucosal nodules with minimal ulceration. In 50 per cent of the cases in which accurate information was available, the tumors were multicentric. There was pronounced infiltration of the submucosa, the muscularis, the peritoneum, the nerves, the lymphatic spaces, and the blood vessels. Puckering and kinking in the region of tumor invasion were observed and may provide a valuable roentgenological sign of identification. Involvement of the regional nodes was observed in 11 cases and hepatic metastasis in 5.

Evidence was afforded on the basis of microscopic studies that all carcinoid tumors are in essence peculiar, low grade (1, Broders) adenocarcinomas. It is suggested, however, that the word "carcinoid" be appended by virtue of customary usage and at the same time perhaps as a designation of the peculiar mode of origin, life history, and spread of these rather unusual neoplasms.

Whipple, A. O., Singleton, A. O., Jones, T. E., Allen, A. W., and Others: Symposium on the Surgical Management of Malignancy of the Colon. *Surgery*, 1943, 14: 321.

Most of the authors participating in this symposium agree that carcinoma of the colon is still an

important public health problem in spite of continued improvements in its surgical management. The major problem in the treatment of this condition is to see the patient and recognize the disease early. At the present time the only manner by which carcinoma of the colon can be cured is by early and adequate resection.

Everyone now generally recognizes the importance of careful preoperative preparation with correction of fluid, electrolyte, and protein balance; the prevention and treatment of shock with plasma and whole blood transfusions; adequate vitamin intake; and sulfonamide therapy, in the improved results of colon surgery. Differences in the treatment of colon cancer are concerned chiefly with the technique of resection and of re-establishment of bowel continuity.

WHIPPLE emphasizes the importance of three fundamental principles in resections of the gastrointestinal tract: (1) the maintenance of an adequate blood supply to the zone of anastomosis by careful preservation of the nutrient vessels in the mesentery, (2) the adequate apposition of peritoneum on either side of the suture line by accurate seromuscular or seroserous suture, and (3) the avoidance of tension on the suture line by decompression of the bowel proximal to the site of suture.

For resections of the terminal ileum, cecum, and right colon, excellent preoperative decompression of the small intestine can be accomplished by the Miller-Abbott tube instead of the older method of proximal enterostomy. The hazards of spillage, contamination, and subsequent leakage are eliminated when the proximal bowel is decompressed, and the open type of anastomosis if done by accurate suture technique is as safe as the closed or aseptic method.

Detailed tables summarize the results obtained in this author's experience by ileocolectomy, by resection and anastomosis, and by the Rankin and Mikulicz procedures for the treatment of carcinoma and other diseases of the large bowel.

SINGLETON presents an excellent review of the anatomical relations between the colon and its blood supply, and illustrates the hazards that may be encountered if one fails to recognize the presence of vascular anomalies.

Based upon the anatomical relations between the colon and the blood vessels which supply it, the following technical suggestions are made:

1. When the bowel is opened in a temporary colostomy the incision should be made at the antimesenteric border between the taenia and in the long axis of the bowel.

2. This area of the colon also should be the site of union for ileocolostomy by the end-to-side or side-to-side anastomosis.

3. A minimal amount of freeing of the mesentery from the bowel wall should be done when making an end-to-end anastomosis of the colon.

4. When resection of the colon is to be followed by end-to-end anastomosis the clamps should be placed across the bowel at a slight angle to avoid any impairment of circulation to the antimesenteric border of the bowel wall.

The importance of the epiploic appendices, the correct method for their ligation, and the value of the omentum in bowel surgery are mentioned.

JONES insists that any change in bowel habit or the presence of bleeding be considered as being due to malignancy until this is disproved.

Any operation for carcinoma of the colon must be as extensive and as radical as possible. The method by which the resection is accomplished is of small importance if the results are equal to those obtained by other methods from the standpoint of mortality and morbidity.

For lesions of the right colon Jones prefers the one-stage right colectomy with ileotransverse colostomy by an end-to-side anastomosis over a Rankin clamp. The two-stage procedure with side-to-side anastomosis between the ileum and transverse colon and resection of the right colon at a later date is used only when there is obstruction or perforation of the growth. The Miller-Abbott tube is substituted for proximal ileostomy whenever possible.

Jones is an advocate of the modified Mikulicz pack when reperitonealization of the right colic gutter is difficult. In this manner adhesions of the small intestine and subsequent obstruction are diminished. A minimal number of wound infections and disruptions is attributed in part at least to figure-of-eight alloy-steel-wire closure.

For lesions in the transverse colon, one-stage resection and primary anastomosis with a complementary tube cecostomy is the procedure of choice. In cases with marked obstruction the cecostomy should be done first, followed in a week by resection. Recently, the Rankin type of obstructive resection has been employed in some cases.

Lesions of the splenic flexure and of the sigmoid are removed by the Rankin obstructive resection when feasible.

When the lower border of the tumor is 3 in. above the peritoneal reflection of the rectum, colostomy followed by resection and end-to-end anastomosis is preferred in young individuals. In people over sixty years of age the anterior resection of Hartman may be used; this is done by dividing the bowel at a safe margin below the growth, turning in the rectum, and bringing the proximal loop out as a permanent colostomy.

When the lesion is in the rectum or rectosigmoid the one-stage abdominoperineal resection of Miles offers the best prognosis, the lowest mortality and morbidity, and the greatest palliation. Jones' remarkable record of over 600 cases with a mortality of 7.2 per cent, and of 128 consecutive cases without a fatality is indeed an enviable one.

ALLEN prefers the term resectability to operability with its implication of cure. He presents the mortality and morbidity statistics from the surgical service of the Massachusetts General Hospital, Boston, where 91 per cent of 186 cases of colon carcinoma were found to be resectable.

The right colon was involved in about 25 per cent of the patients. A resection in this area is more apt to be followed by cure because of the ease with which the entire vascular and lymph-node area may be included in the resection. The operative mortality, however, is high. The recommended procedure is a two-stage resection with a preliminary aseptic or closed ileotransverse colostomy followed by resection at a later date.

The transverse colon was involved in about 11 per cent of the patients. If the lesion was in the proximal third of this segment it was treated by the same method as a lesion in the right colon. If the midportion of the transverse colon is involved a preliminary ileocolostomy is a handicap and the one-stage resection is conceded to be preferable.

Lesions in the distal transverse colon, the splenic flexure, and the upper descending colon are rare and tend to metastasize late. They are treated by preliminary cecostomy followed by resection and closed anastomosis, although obstructive resection may be justified.

The lesion was found in the sigmoid in 53.9 per cent of the cases. Here resectability is good and operative mortality low, but the cure rate of survivors is poor, probably because of earlier lymphatic spread and liver metastases. Many of these patients have complete obstruction which may be relieved by cecostomy or proximal loop colostomy. Ten days later resection and aseptic anastomosis may be done.

The value of succinylsulfathiazole therapy in the preoperative preparation of patients is emphasized. The Miller-Abbott tube has been found of great value in the preparation and postoperative care of these patients. Delayed closure of the abdominal wound forty-eight hours after resection by Coller's technique or a modification of it is recommended.

ZINNINGER and HOXWORTH review the statistics from the Cincinnati General Hospital, Cincinnati, Ohio, and illustrate the difference in operability between patients in a private hospital and those in a general hospital. Resectability is much greater in private patients.

The general plan of management is given for all patients who are admitted to the hospital with signs of intestinal obstruction.

In uncomplicated lesions of the cecum, ascending colon, or hepatic flexure, a one-stage resection is done with a side-to-side or end-to-side anastomosis. The technical steps involved in these procedures are explained and illustrated in excellent detail.

Lesions distal to the hepatic flexure, exclusive of the rectum, are removed usually by resection and end-to-end anastomosis.

A mortality of 8.8 per cent was reported for 45 cases of resection for carcinoma of the colon, not including lesions of the rectum.

CATTELL reports on 503 patients treated for carcinoma of the colon and rectum at the Lahey Clinic, Boston. The sex and age incidence, the duration of symptoms, and the location of the lesions are analyzed. At the time of operation one-third of the lesions showed no evidence of metastases. There was involvement of the lymph nodes in 40 per cent of the cases, blood-vessel invasion in 31.8 per cent, invasion of other organs in 22.2 per cent, and liver metastases in 9.6 per cent. Four hundred and twenty of the patients underwent some type of resection, a resectability rate of 83.5 per cent.

For carcinoma in any region of the colon except the rectum and rectosigmoid the two-stage modified Mikulicz resection is considered the procedure of choice at this clinic. One hundred and thirty-three cases of this type were operated upon with a mortality of 11.3 per cent.

For carcinoma of the rectum and rectosigmoid, the one-stage abdominoperineal resection of Miles is considered the operation of choice in good risk patients and was performed in more than half of the cases, with a mortality of 6.5 per cent. One-third of the cases (patients with obstruction or perforation, or poor-risk patients) had two-stage abdominal resections according to Lahey with a mortality of 13.8 per cent. A one-stage abdominal resection was performed in a few cases, leaving a small rectal stump in place, with a mortality of 23.5 per cent. An additional few poor-risk patients with low rectal lesions had two-stage resections with a loop colostomy and then perineal resection, with 20 per cent mortality.

The end-results following 162 resections in patients who were followed for from five to ten years showed that 46.3 per cent survived between five and nine years, 13.5 per cent died postoperatively, 40.2 per cent died of recurrence, and 53.6 per cent showed no evidence of recurrence.

DAVID discusses the management of polyps which occur in the rectum and colon. The generally accepted relationship between rectal and colonic polyps and malignancy is again emphasized.

Pedunculated adenomas which can be prolapsed through the anus are removed by ligation of the pedicle well away from the adenoma. Those which can be seen by proctoscopic examination may be removed by thorough fulguration of the pedicle with a long fulguration wire enclosed in a ureteral catheter. Flat adenomas below the peritoneal reflection can be fulgurated and carbolized with safety. Adenomas above the peritoneal reflection must be removed by laparotomy after careful preparation of the patient for resection in case it should be necessary.

For large sessile papillomas in the ampulla of the rectum not suitable for fulguration and difficult to approach from above or below, a method of operative removal is described in which the rectum is split open up to the coccyx to permit removal of the lesion, followed by closure of the bowel wall and sphincter in layers.

Multiple polyposis of the colon should be treated by graded colectomy.

WAKELY describes the coldlight sigmoidoscope and stainless-steel inspection mirror which he has used recently with very satisfactory results for all sigmoidoscopic and proctoscopic examinations.

FALLIS suggests a re-evaluation of anterior resection of the rectosigmoid and upper rectum with establishment of bowel continuity by end-to-end anastomosis. This procedure is advocated for tumors of the low sigmoid colon, in certain poor-risk patients, as an alternative for the classical abdominoperineal resection of Miles in cases of borderline operability, and when permanent colostomy is refused. The rationale, technique, complications, and results of the procedure are discussed.

WANGENSTEEN presents the current practice in the University of Minnesota Surgical Clinic, where an attempt is made to resect all unobstructed lesions of the colon in one stage and re-establish bowel continuity by oblique end-to-end closed or aseptic anastomosis. No decompressive vents are used except the indwelling duodenal tube.

In addition, a preliminary report is made of his experience with abdominoanal methods for the restoration of bowel continuity, with preservation of the rectal sphincters, after excision of carcinomatous lesions of the rectal ampulla.

EDWARD W. GIBBS, M.D.

LIVER, GALL BLADDER, PANCREAS, AND SPLEEN

Herbert, F.: Prothrombin Deficiency in Biliary Obstruction and Diseases of the Liver. *N. England J. M.*, 1943, 229: 265.

The author presents his experience with the two-stage method of estimating the plasma prothrombin in obstructive jaundice, and diseases of the liver. The main contribution is additional evidence concerning the incidence of hypoprothrombinemia in these conditions, based on an accurate technique (the technique of Warner and his associates). He also presents examples of the correction of the prothrombin deficiency by treatment in cases of obstructive jaundice, and the lack of response in liver disease.

In the patients with biliary obstruction with moderate or intense jaundice the prothrombin titer before treatment with 2-methyl -1, 4-naphthoquinone by injection, was normal in only 16 of 51; the level was between 50 and 80 per cent of normal in 19 and below 50 per cent of normal in 16. There was no regular correlation in this group between serum bilirubin and prothrombin or between phosphatase and prothrombin. There was a definite correlation between the prothrombin titer and the duration of obstruction. Although gross reductions are sometimes found at an early stage, it is usual during the first four weeks to find normal or moderately low values, whereas after four weeks the titers are all low and the grosser deficiencies much more frequent. In only 1 case of obstructive jaundice was the response to the intramuscular injection of 2-methyl-1, 4-naphthoquinone unsatisfactory, and the author considered the lack of response as probably being due to invasion of the liver by metastasis from a carcinoma of the pancreas.

In liver diseases 27 of 40 patients showed a prothrombin deficiency. In acute or subacute hepatitis the prothrombin levels varied from 17 to 106 per cent of normal with 7 of the 18 cases showing normal levels and most of the remainder showing moderate deficiencies, only 3 having titers below 56 per cent of the normal average. In 2 cases of liver atrophy, there was a severe deficiency of prothrombin. Of 12 cases of cirrhosis, 3 were normal and only 2 had a titer below 50 per cent of normal. In 2 cases of atrophic fibrosis there was a considerable deficiency. In the cases of liver damage given 2-methyl-1 4-naphthoquinone, the response was less than for obstructive jaundice. EARL O. LATIMER, M.D.

Dessau, F. I.: The Incidence of Gallstones in the Higher Age Groups. *N. England J. M.*, 1943, 229: 464.

The author examined the post-mortem records of the Long Island Hospital, Boston, to determine the incidence of gallstones in the higher age groups, i.e., in individuals more than forty years of age. Of 2,791 post-mortem examinations of patients over the age of forty, 20.9 per cent revealed stones in the gall bladder, while of 451 examinations of patients below the age of forty, 1.5 per cent revealed stones in the gall bladder. The incidence was found to increase with age. Between the ages of forty-one and sixty years the incidence was 8.4 per cent among males and 19.1 per cent among females; between the ages of sixty-one and eighty years it was 16.6 for males and 31.2 per cent for females; and above the age of eighty-one years, 26 per cent of the males and 40.3 per cent of the females had stones.

Between the years 1900 and 1922 there was a total incidence of cholelithiasis of 18.9 per cent, with 10.3 per cent in males and 24.5 per cent in females; while between 1923 and 1942 there was a total incidence of 22.2 per cent, with 17.0 per cent in males and 32.7 per cent in females. Cholecystitis was present in 42 per cent of the males and 34 per cent of the females who had gallstones.

EARL O. LATIMER, M.D.

Holman E., Wood, D. A., and Stockton, A. B.: Unusual Cases of Hyperinsulinism and Hypoglycemia. *Arch. Surg.*, 1943, 47: 165.

Masses of aberrant pancreatic tissue varying greatly in size have been described. The recorded locations of such aberrant tissue are shown in Table I.

Exceedingly variable symptoms are attributable to these anomalies. They may be those due to simple ulcer, such as anorexia, nausea, vomiting, epigastric pain, insomnia, and loss of weight, or those due to appendicitis, cholecystitis, or diverticulitis. Symptoms of obstruction due to intussusception or even suspected cancer of some intra-abdominal organ have been described. In none of the tabulated cases have the symptoms of hyperinsulinism been associated with aberrant pancreatic tissue.

Recorded, however, in the literature, are 4 cases of extrapancreatic islet adenomas producing symp-

TABLE I.—LOCATIONS OF ABERRANT TISSUE

Stomach	95
Duodenum	105
Duodenojejunal angle	2
Jejunum	65
Ileum	18
Small intestine	6
Diverticulum of stomach	3
Diverticulum of duodenum	7
Diverticulum of jejunum	1
Diverticulum of ileum	8
Diverticulum of small intestine	2
Meckel's diverticulum	21
Diverticulum (not located)	1
Umbilical fistula	1
Mesentery	3
Omentum	4
Splenic capsule	3
Spleen	1
Gall bladder	3
Cystic duct	1
Gastrocolic ligament	1
Transverse mesocolon	1
Location questionable	18
Total	370

toms of hyperinsulinism and hypoglycemia which were entirely controlled by removal of the extrapancreatic adenomas. To these 4 the authors add a fifth case, in which the removal of one intrapancreatic adenoma failed to relieve the hypoglycemic symptoms, but the removal of a second islet adenoma in the gastrosplenic ligament produced complete cure.

This case led the authors to the conclusions that:

1. The presence of one tumor does not exclude the existence of a second.

2. In patients who have been proved to have hypoglycemia and who exhibit Whipple's "essential triad: attacks of central-nervous-system disorder motor, vasomotor, or psychic coming on during the fasting state; fasting blood-sugar levels of 50 mgm. per cent or less; and immediate recovery from these attacks on the administration of glucose by mouth or by vein," failure to find an intrapancreatic tumor after complete and thorough search of the entire pancreas should be followed by a wide search for abnormal masses in the localities where extra-pancreatic tissue is most frequently found.

A case of heterotopic islet adenoma of the duodenum without hypoglycemic symptoms, and a case of islet carcinoma apparently engrafted on a calcified islet adenoma which presumably had been responsible for hypoglycemia of varying severity over a period of sixteen years, are presented in detail.

Likewise, a bizarre case of hypoglycemia characterized by episodes of unconsciousness and a low blood sugar of 33 mgm. per 100 cc. values is reported; no pathology was discovered at operation, but there was complete freedom from all hypoglycemic symptoms after the operation.

The authors apologetically refrained from offering any explanation for the astonishing result.

STEPHEN A. ZIEMAN, M.D.

Rockey, E. W.: Total Pancreatectomy for Carcinoma. *Ann. Surg.*, 1943, 118: 603.

The author reports a case of carcinoma of the pancreas in which a total pancreatectomy was performed. The patient died on the fifteenth postoperative day of a chemical peritonitis due to bile.

The pancreatectomy was performed in two stages, the first being done on June 19, 1942 and the second, three days later. At the first operation a massive carcinoma of the body of the pancreas was found, which seemed to extend to the tip of the tail of the pancreas and irregularly into the head. A palliative cholecystoduodenostomy was performed. At the second operation the cholecystoduodenostomy was taken down. The entire pancreas, the lower half of the stomach, and the entire duodenum were removed in one piece (Fig. 1). An anterocolic isoperistaltic anastomosis was made between the jejunum and the open end of the stomach. An anterocolic anastomosis was then made between the jejunum, at a point 8 in. distal to the gastrojejunostomy, and the previously made opening in the fundus of the gall bladder (Fig. 2). A cigarette drain was brought out through a stab wound to the right of the main incision from the region of the stump of the ligated common duct.

Pathological diagnosis of the surgical specimen was adenocarcinoma of the pancreas in association with distinctive fibrosis.

The postoperative course of the patient with reference to insulin dosage, glucose administration, and diet is summarized in Table 1.

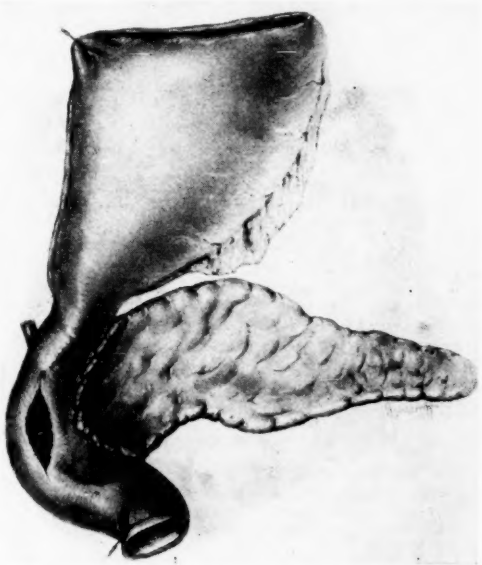

Fig. 1. Drawing of the operatively removed specimen, the lower half of stomach, and entire duodenum and pancreas.

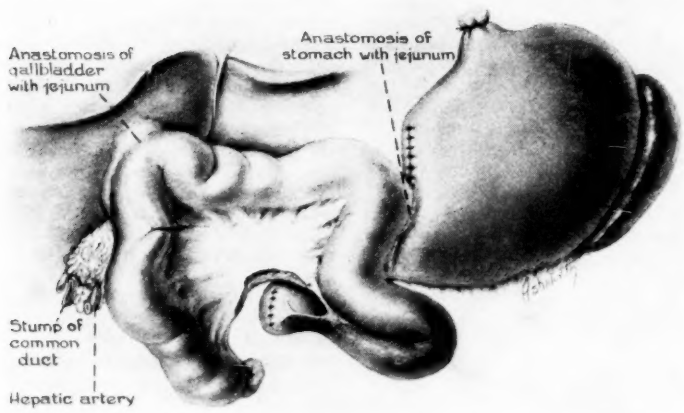

Fig. 2. Drawing of the autopsy specimen. The hepatic artery had been divided post mortem. (Courtesy of J. B. Lippincott Co.)

TABLE I.—SUMMARY OF POSTOPERATIVE COURSE WITH REFERENCE TO INSULIN DOSAGE, GLUCOSE ADMINISTRATION, AND DIET

Day of Operation
- Total insulin dosage—67 units
  - 17 units before surgery
  - 25 units 5:15 PM
  - 25 units 7:00 PM
- Blood sugar—250 mgm. at 3 PM
- Glycosuria—3 plus at 4 PM
- Total I.V. glucose (5%)—1700 cc.

1st Postoperative Day
- Total insulin dosage—93 units
- Blood sugars— 72 mgm. fasting; 40 mgm. 12 M; 40 mgm. 5 PM; 212 mgm. 7:15 PM } severe and prolonged insulin reactions
- Glycosuria—none in 24 hour specimen for this day.
- Total I.V. glucose—2000 cc. (5%)
  50 cc. (50%)—this was given in 2 injections, 25 cc. at 12:45 PM, and 25 cc. at 3:00 PM.

2nd Postoperative Day
- Total insulin dosage—12 units
- Blood sugar—80 mgm. fasting
- Glycosuria—23 gm. in 24 hour specimen for this day.
- Total I.V. glucose—2000 cc. (5%)
  10 cc. (50%)
- Total I.V. saline solution—1000 cc.

3rd to 14th Postoperative Day
- Insulin dosage raised to high of 27 units
- Glycosuria—0 to 24 gm. (24 hour)
- Blood sugars—200 to 286 mgm.
- Alkali reserve—45—(14th p.o. day)
- Feedings—C- P- F-
  100 60 60 throughout this period.

No evidence of ketonuria at any time during postoperative period.

Except for a severe hypoglycemic reaction with violent convulsions and unconsciousness on the first postoperative day the course was uneventful until the tenth postoperative day when bile seepage from the drainage tract was observed. On the thirteenth postoperative day atelectasis of the left lower lobe of the lung occurred. On the fourteenth postoperative day signs of peritonitis developed. The general condition became progressively worse and the patient died on the fifteenth postoperative day.

The explanation of the low insulin requirement in this patient is obscure.

Post-mortem examination revealed a large amount of serofibrinous bile-stained exudate in the peritoneal cavity. The anastomoses were in good condition. The ligated end of the common duct was not identified; apparently it was open. The liver showed no fatty infiltration. A small piece of pancreatic tissue was found lying between the stump of the common duct and the hepatic artery. This weighed slightly less than 1 gm.

Because the blood supply of the common duct comes from the inferior end of the posterior superior pancreaticoduodenal artery the author believes that implantation of the common duct into the jejunum is probably a safer and wiser procedure. This would tend to give the stump of the duct an additional blood supply from the jejunal tract.

DWIGHT E. CLARK, M.D.

MISCELLANEOUS

Kelly, E. C.: Nonpenetrating Abdominal Trauma. *Surgery*, 1943, 14: 163.

This article contains a review of the incidence and mortality rate of nonpenetrating abdominal trauma during the fifteen years from January 1, 1927 to December 30, 1941 at the Albany Hospital, Albany,

New York. This is a general hospital of about 600 beds, receiving the usual proportion of highway, home, and industrial accidents. A study of nonpenetrating abdominal trauma in this institution should, therefore, indicate the frequency and seriousness of these injuries.

The total number of admissions during this fifteen-year period was 157,344. Of this total, 74 patients had nonpenetrating abdominal traumas. These 74 patients were distributed among 21 doctors who saw very few patients with this type of injury. There was no uniformity in the treatment. Of the 74 persons, 33 died, which brought the mortality rate up to 44 per cent.

It might be interesting to mention other serious traumas by way of comparison. During this same period 269 patients were admitted with fracture of the vertebrae, and 207 patients with fractures of the pelvis. It is therefore apparent that the incidence of nonpenetrating abdominal trauma is small but that the mortality rate is very high.

Using a set of statistical tables the author proceeds with his survey, setting forth the type of lesion with the number of patients who died or recovered, and the mortality percentages.

The kinds of complicating lesions in this review of 74 cases comprise 5 cases of rupture of the urinary bladder with a mortality rate of 60 per cent; 13 cases of rupture of the intestine with a mortality of 69 per cent; 29 cases of kidney injuries with a mortality of 10 per cent; 16 cases of rupture of the liver with a mortality of 75 per cent; 1 case of rupture or tear of the mesentery with recovery; 9 cases of rupture of the spleen with a mortality of 55 per cent; and 1 case of rupture of the stomach with a mortality of 100 per cent.

One table shows the type of lesion year by year, and shows that a specific type of lesion may be found only at intervals of several years. Another table gives the type of injuries received and shows that 55 per cent of the patients were injured as the result of automobile accidents.

The final table shows the mortality rate by five-year periods. There has been a marked drop in the mortality rate in the past five years, which indicates that considerable improvement has taken place. This improvement is in part due to prompt operation of the later cases and, in part, to the use of some type of sulfa drug in the chemotherapy.

The author believes that the mortality occurring in cases of this type should be decreased by the following:

1. Proper training of first-aid workers, interns in accident room and wards, as well as of doctors
2. Use of plasma in shock
3. Operation within six hours if indicated
4. Proper use of the sulfa drugs intraperitoneally.

MATHIAS J. SEIFERT, M.D.

GYNECOLOGY

UTERUS

Manstein B.: The Occurrence of Double Cancer in the Uterus (Ueber das Vorkommen von Doppelcarcinomen am Uterus). *Arch. Gyn.*, 1942, 174: 153.

Simultaneous occurrence of squamous-cell and adenomatous carcinoma in the uterus is extraordinarily rare.

A thirty-eight-year-old woman was admitted with complaints of metrorrhagias and lumbar pain. The gynecological examination revealed a cauliflower tumor of the cervix and a large corpus uteri. A radical Wertheim operation was performed. The inspection of the removed specimen showed cancer of the cervix not extending beyond the internal os. In the corpus uteri the normal mucosa was replaced by polypoid formations. The histological examination revealed a squamous-cell carcinoma of the cervix and adenocarcinoma. Both tumors were well separated from one another.

Cases have been published in which two different tumors have been found in the cervix. According to the embryological development of the cervix, a primary carcinoma may originate from the squamous epithelium of the sinus urogenitalis or from the cylindrical epithelium of the cervical canal which develops from Mueller's ducts. As to the origin of squamous cells in the corpus uteri, there is no unanimity of opinions: while some workers believe that they are dealing with cells displaced during the embryonal life, others are of the opinion that the cells develop from indifferent zones of growth. The fact has been definitely established that no direct metaplasia takes place in fully developed glandular or squamous epithelium.

According to the author's opinion, the carcinogenic factor provokes the development of a cancer not necessarily in fully differentiated, functioning epithelium but in cells with pluripotent possibilities. Uterine epithelium originating from Mueller's ducts may develop in both directions. Even if double carcinoma forms two distinct tumors separated from one another, their origin from the same embryonal "anlage" must be considered. A diagnosis of double origin should be made only if both tumors do not resemble each other histologically and do not form from the same embryonal basic tissue. Not only cylindrical but also probably squamous epithelium may develop from the embryonal "anlage" of Mueller's ducts. The cervical epithelium originates from the sinus urogenitalis. Two cancers of the uterus with different histological structures may originate from the same pluripotent mother cells. Only if a common origin can be excluded, a diagnosis of primary double tumors is justified. Unfortunately this demand cannot be met by available methods of investigation at the present time.

JOSEPH K. NARAT, M.D.

EXTERNAL GENITALIA

Karnaky, K. J.: The Use of an Acid Jelly Postoperatively after Vaginal and Cervical Operations and in Nonspecific Injections of the Vagina. *Texas J. M.*, 1943, 39: 178.

Operations on the vagina or cervix are followed by secondary vaginal infections. This type of postoperative infection is in no way different from the ordinary vaginal infection. It has been shown that in the vagina after operation there is an abnormal change in the acidity pH, glycogen content, bacterial flora, and epithelial-cell height. These phenomena also occur in typical cases of vaginitis.

The best method for the treatment of an infected vagina, particularly in nonspecific infections, is by acid applications. The vagina should be treated similarly after operation.

The acid jelly is an excellent agent for postoperative treatment of the cervicitis, also following surgery for cystocele and rectocele, vaginal hysterectomy, and after all vaginal operations. The method is convenient and painless. The jelly adheres well to the vaginal vault and, being highly buffered, effectively neutralizes the abnormal vaginal and cervical secretion. The acid jelly used in this study was nontoxic and non-irritating.

After the initial instillation of the acid jelly, postoperatively, one to two doses of the jelly are inserted deep into the vaginal vault night and morning for at least fifteen days. Immediately following a conization of the cervix a cotton plug is packed in the coned area. Acid jelly and cotton balls are packed well in the vagina, two to three times a week for the first week, twice the second and third weeks, and then as needed. Cotton stimulates while gauze irritates the vagina. Sutures remain in place longer if the vagina is kept acid with jelly; hence, the number of postoperative failures should be lessened.

CHARLES BARON, M.D.

MISCELLANEOUS

Dick, A. C.: Menstrual Exercises. *Indust. Med.*, 1943, 12: 588.

The author discusses the problem of dysmenorrhea with reference to industrial medicine, and the part that dysmenorrhea plays in absenteeism and in diminished work efficiency at the Consolidated Vultee Aircraft Corporation, San Diego, California. The method of treatment was that advocated by the University of California at Los Angeles and the Los Angeles City School System. It is essentially an exercise for active, progressive, ligamentous stretching. The treatment was used throughout a ten-month period by the Vultee Aircraft Corporation, and during that period 70,000 absentee hours due to dysmenorrhea were eliminated and an additional

70,000 hours were gained in the work of the women who had been suffering from dysmenorrhea but had not been taking time off. The series consisted of 353 women and the findings are tabulated.

The need for this treatment is based upon the fact "that in women suffering with dysmenorrhea there is a postural defect of contracted fascial ligamentous bands restricting posterior tilt excursion range of the pelvis in relation to the legs and back." Then upon menstruation the ligaments further shorten and produce pressure and irritation of the contiguous nerves. The specific spinal nerves are the eleventh and twelfth dorsal, and the first lumbar. The treatment is directed toward reducing and relieving this pressure and irritation of these nerves. The exercise is as follows:

"The patient stands with heels and toes together about 18 in. from, and with side to, a wall. The elbow is placed against the wall at shoulder level, with the forearm and hand resting on the wall. The heel of the opposite hand is placed in the hollow on the posterior aspect of the greater trochanter of the hip. The shoulders are kept in a line with the elbow perpendicular to the wall and not allowed to shift forward. The knees are kept completely extended and not allowed to flex. The abdominal and gluteal muscles are strongly contracted while the hips are shifted slightly forward and in toward the wall, aided by pressure on the greater trochanter of the femur from the heel of the hand. The objective is to force the extent of sideward and forward shift of the hips in toward the wall far enough not only to place a strain on the contracted ligamentous bands but to gain a progressive stretch as well. This accentuates the symptoms momentarily at each stretch. The stretchings are done routinely, three times to each side at three periods daily, a total of 9 stretchings to each side every twenty-four hours."

The program is augmented by constant supervision of the exercises and close co-operation with the medical staff. Furthermore, it was found that the program was considerably enhanced by the use of bulletin-board reminders. In addition, at the time of employment the women were studied carefully for symptoms of dysmenorrhea, and the value of co-operation with health measures was stressed.

ROBERT LICH, JR., M.D.

Macht, D. I.: Further Historical and Experimental Studies on Menstrual Toxin. *Am. J. M. Sc.*, 1943, 206: 281.

A comprehensive review of the literature relative to the presence of a menotoxin is presented in addition to considerable original work on the subject. It is pointed out that experimentally and clinically much evidence can be collected to substantiate the folk lore relative to the menstruating woman.

The psychological, pathological, and physiological variation in the female seems closely correlated to catamenia, but there are two schools of thought as to the modus operandi: first, those that offer an endocrinological explanation and, second, those that suggest the activity or failure of elimination of the menotoxin as the responsible agent.

The menotoxin is found in the serum and plasma of the female and also in such secretions as sweat, saliva, and milk. Since the physiological or pathological disturbance in women is most evident in the immediate premenstrual phase it is assumed that menstruation affords an outlet to this toxin. This is demonstrated experimentally and it is suggested that this phenomenon may offer an explanation for the therapeutic failures in sex endocrinology. Also, this affords insight into the disturbance and unsatisfactory results so often experienced with hysterectomy even when the ovaries are left intact.

Chemically, menotoxin seems to be closely related to oxycholesterol, and ovarian hormones, too, indicate a similar relationship. This chemical similarity was supported by the author's phytopharmacological methods, in which he demonstrated an increased cellular activity with crystalline estrone as compared to cellular inhibition with crystalline progesterone.

The article is presented in a most logical and complete form with illustrations of experimental work and a complete bibliography. The subject is discussed from an experimental standpoint and clinical applications are noted. ROBERT LICH, JR., M.D.

Adams, T. W.: Ureteral Injury During Gynecological Surgery. *West. J. Surg.*, 1943, 51: 305.

The author summarizes 2 previously reported series of ureteral injury in gynecological procedures. These reports cover the literature up to 1936. He has studied the American literature from 1936 to 1941 and has found 73 cases and adds 3 additional ones.

Ureteral injury in gynecological procedures occurs in about 0.4 per cent of the cases. However, it is a known fact that ureteral injury is frequently unrecognized. Newell reported 15 such cases, 6 of which were not recognized until they were found at autopsy.

In the present series 50 cases were unilateral injuries, and 17 were bilateral. The incidence seems to be about the same for both sides.

It is frequently difficult to determine the exact cause of the ureteral injury as the condition is often not discovered until so much time has elapsed that the exact type of injury cannot be diagnosed. There are five general types of injury: (1) ligation; (2) incision; (3) excision; (4) necrosis, and (5) obstruction from surrounding postoperative edema and inflammation. A ureteral fistula following injury may make its appearance any time between the first and thirty-fourth postoperative day. There is no set time when this may occur.

In regard to the treatment, the author is of the opinion that when the injury is recognized during the course of an operation, immediate restoration of the kidney-bladder continuity should be attempted. As previously mentioned, the recognition of injury is not frequent at the time of operation. In the present series it occurred only 8 times in the operative

period, whereas it occurred 67 times during the post-operative period.

When the ureter has been severed the two procedures of choice are ureteroureteral or ureterovesical anastomosis. In most instances the location of the damage will determine the choice of operation to be used. Many types of anastomosis have been devised: (1) transverse end-to-end; (2) transverse end-in-end; (3) end-in-side; (4) oblique end-to-end; (5) side-to-side; and (6) a combination of end-to-end and side-to-side. Peterson in grouping his series favored the telescoping type of operation. The author discusses the value of leaving a ureteral catheter "in situ" to be removed later through the bladder; he believes that this acts both as a splint for the repaired ureter and affords drainage.

When neither of the procedures mentioned can be carried out, implantation of the ureter into the bowel may be employed. Another suggestion has been the transureteroureteral anastomosis. Two cases of this type are reported in the series with excellent results. Voluntary ligation of the ureter is recommended by the author only when the patient is in such poor condition that further operative procedure will seriously endanger her life. When this is done it must be done with full knowledge that the end-result will be atrophy of the kidney, hydronephrosis with subsequent nephrectomy, leakage, either with infection or fistula formation, or, in the occasional case, reflex urinary suppression associated with uremia and death.

The great difficulty in deciding which is the best type of operation lies in the fact that most cases have not had a sufficiently long follow-up. This follow-up must include visualization of the entire kidney tract to rule out ultimate ureteral stricture at the site of repair with secondary hydroureter and hydronephrosis above the point of injury.

When the ureter is not cut but only clamped or ligated and it is recognized at the time of operation, the clamp should be removed or deligated immediately. The integrity of the ureteral wall may be jeopardized even when clamps or ligatures are left on the wall for a short time. This may be followed by necrosis or fistula formation. Therefore, when any doubt of ureteral integrity exists it is best to excise the damaged portion and make a ureteroureteral or ureterovesical anastomosis.

Of the 8 cases of ureteral injury recognized at the time of operation in this series, 2 were treated by ureterovesical anastomosis with 1 good result and 1 instance of ureteral stricture and kidney atrophy. One case was treated by ureteral implantation into the bowel with good results. In 5 cases ureteroureteral anastomosis was attempted. Good results were obtained in 3. There was 1 case of failure in which the function was good after ureteral dilatation, but it became necessary for other reasons to place the patient in a body cast for a year and a ureteral stricture resulted. There was 1 death.

There are probably many cases of unrecognized unilateral ligation of the ureter with an asymptomatic atrophy of the affected kidney. This condition may pass unnoticed unless kidney investigations happen to be carried out at a later date. On the other hand, leakage may occur and result in local or general infection or in fistula formation. It is this latter complication by which the unrecognized cases of unilateral damage usually make themselves known. In 34 of the 50 cases of unilateral injury in this series, the first indication that the ureter had been injured was the fistula formation. Bilateral occlusion of the ureter cannot go unrecognized for long. The symptoms are anuria and gradually developing uremia. Failure to obtain urine from the bladder in twelve hours following pelvic surgery calls for immediate investigation. Should this prove bilateral ureteral occlusion, immediate steps for drainage must be undertaken.

There are two general methods of attack: (1) the re-establishment of the ureteral tract drainage; and (2) the temporary substitution of drainage above the point of injury by either unilateral or bilateral nephrostomy or ureterostomy.

From a study of the cases in the literature it would seem that the treatment of any case of bilateral injury should be aimed at the preservation of life and restoration of kidney function until nature or a well planned operative procedure can rectify the ureteral damage.

The author reports 3 cases, 1 of his own and 2 from his colleagues, with clinical data.

In conclusion, he states that ureteral injury occurs seldom in the experience of any one operator and for this reason knowledge of sequelae and treatment can be obtained only through the study of collected cases. Such an analysis has been presented. The results are sufficiently encouraging to warrant the re-establishment of ureteral continuity rather than to sacrifice the kidney. It cannot, however, be too strongly emphasized that a worth-while estimation of results can be made only when long time follow-up studies of the kidney function are included in the case reports.

HENRY C. FALK, M.D.

OBSTETRICS

PREGNANCY AND ITS COMPLICATIONS

Byrn, J. N., and Eastman, N. J.: Vitamin A Levels in Maternal and Fetal Blood Plasma. *Bull. Johns Hopkins Hosp.*, 1943, 73: 132.

The Vitamin A level was determined in the blood plasma of 297 women at term and in 14 women at various intervals during the course of pregnancy. In 50 cases the vitamin A level of the fetal-cord blood was also obtained. The determinations were made on samples of oxalated blood plasma by the alcohol precipitation method recommended by Yudkin and adapted to the Klett colorimeter. Dilutions of U. S. P. reference cod-liver oil in chloroform and of beta-carotene in petroleum ether were used to plot the standard reference curves.

Vitamin A depletion is not a common cause of obstetrical complications among metropolitan dispensary groups.

There are substantial amounts of vitamin A and traces of carotene in fetal plasma. The fetal values, however, cannot be raised by increasing the maternal vitamin A or carotene levels. The method of placental transfer of vitamin A is still unknown.

CHARLES BARON, M.D.

Watts, R. M., and Adair, F. L.: The Excretion of Estrogen and Gonadotropin in Late Pregnancy. *Am. J. Obst.*, 1943, 46: 183.

The excretion of estrogen and gonadotropin was determined in 74 cases during pregnancy; 70 cases were studied during late pregnancy (thirty-five weeks) and 4 cases in early pregnancy. Of the 70 cases studied in late pregnancy, 57 were used for a statistical study of the relation of these hormones to the toxemias of pregnancy. Of these, 43 cases (11 normal, 14 hypertensive with renal disease, 13 pre-eclamptic, and 5 eclamptic) had parallel quantitative assays of both estrogens and gonadotropins, and 14 had assays of estrogen only. The other 13 cases represented various other conditions complicating pregnancy. In the group of 43 cases in which both the estrogens and gonadotropins were determined, there was a decrease in the estrogen excretion and an increase in the gonadotropin excretion in the pre-eclamptic and eclamptic groups, but the excretion of estrogen was normal and that of gonadotropin increased in the hypertensive and renal-disease group. Because of the extreme variability of individual values, the relationship of the estrogen and gonadotropin excretions (E:G ratio) is believed to be a better index of hormone values than the twenty-four-hour excretion for either hormone. The values found are given in detail.

Methods for the quantitative assay of estrogens and gonadotropins employing dose-effect standardization curves and methods of extraction are described and discussed. The excretion of estrogen and gonadotropin has been studied in 17 additional cases representing the following conditions: early pregnancy, hyperemesis gravidarum, abruptio placentae, hysteria with polyhydramnios and partial separation of the placenta, epilepsy, death of the fetus, diabetes insipidus, diabetes mellitus, edema, achondroplastic dwarfism, and pseudomucinous cystadenoma of the ovary.

EDWARD L. CORNELL, M.D.

Torpin, R., and Holmes, L. P.: The Influence of the Placental Site Upon Fetal Presentation. *Am. J. Obst.*, 1943, 46: 268.

The great majority of placentas in human beings are located upon the anterior or the posterior wall of the uterus. The ratio found in this study was 45 anterior to 55 posterior. These figures are exclusive of placentas of other sites which are relatively infrequent.

The placenta located on the anterior uterine wall had a definite tendency to occur with occiput-posterior presentation of the fetus. Mathematically, when the placenta was anterior, the chance for occiput-posterior presentation of the fetus was double that when the placenta was posterior (25.8 per cent to 11.5 per cent).

The placenta located on the posterior uterine wall had an increased tendency to occur with occiput-anterior presentations of the fetus. When the placenta was on the posterior wall, the chance for occiput-anterior presentation was twice that when the placenta was anterior (58.5 per cent to 29.5 per cent). The incidence of occiput-transverse presentation of the fetus in the first stage of labor was 30 per cent when the placenta was located on the posterior wall and 44.7 per cent when it was located on the anterior wall.

EDWARD L. CORNELL, M.D.

Rattner, H.: The Treatment of Syphilis in Pregnancy by the Five-Day Massive-Dose Method. *Am. J. Obst.*, 1943, 46: 255.

Twenty-seven pregnant women with syphilis were treated by the five-day massive-dose method of chemotherapy. In the majority of these cases a modified technique was used in which both arsenic and bismuth were administered concurrently during the five-day period. The treatment was well tolerated by both mother and fetus regardless of the stage of the pregnancy or the duration of the syphilis, whether primary, secondary, or latent. In no instance was there encountered a severe reaction or interference with the pregnancy.

Of the 27 patients, 1 was lost from observation; 25 have given birth to full-term, normal infants; and 1 gave birth to a syphilitic infant after having apparently acquired a second infection while the infant was still *in utero*.

In addition to this group, 5 other patients who had been treated for early syphilis by the massive-dose

method, later became pregnant and gave birth to normally developed seronegative infants, although further antisyphilitic treatment was purposely withheld from the mothers.

The results of the treatment upon the mothers' syphilis were similar to the results obtained in nonpregnant patients treated by the same method for similar types of syphilis.

EDWARD L. CORNELL, M.D.

LABOR AND ITS COMPLICATIONS

Lazard, E. M.: Twenty-Nine Years of Experience with Cesarean Section. *West. J. Surg.*, 1943, 51: 356.

Lazard reports 395 cesarean sections among his own patients, in consultation cases, and on his general hospital service in Los Angeles.

There were 11 maternal deaths, an uncorrected mortality of 2.78 per cent. Of the 395 cases, 158 were his own, 160 were consultation cases, and 77 were general hospital cases. There were 2 deaths in his own cases (1.26 per cent); 4 deaths in the consultation cases (2.50 per cent); and 5 deaths in the General Hospital cases (6.5 per cent). The causes of death were pulmonary embolism (2), sepsis and/or peritonitis (5), uremia (1), and shock (3).

The last death after cesarean section in this group of cases occurred in 1938, since which time there have been 92 consecutive cases in this series without mortality. The classical sections had the highest mortality, 9.2 per cent of 54 cases; the last classical section was done in 1926.

Fetopelvic disproportion, the orthodox indication for section, was noted as the indication in 231 patients; previous section in 72, and in all but 1 of these it had been done previously because of fetopelvic disproportion; transverse presentation in 1, a gravida-1; previous stillbirths in 2; and birth injuries of previous babies in 3, all of which injuries were caused by feto-pelvic disproportion. So that in the 395 cases, feto-pelvic disproportion was the causative factor in 309, or 78.2 per cent. Other less frequent indications were toxemia (20), placenta previa (14), cervical stenosis (14), fibroids (12), ablatio placentae (9), and sterilization (5).

Elective section for the purpose of sterilization is only justified when the medical condition is such as to render further pregnancies dangerous to the mother's life and when the patient cannot or will not practice proper contraceptive methods.

The gross fetal mortality was 4.27 per cent. Fetal mortality at time of section is usually due to the necessity of operating before fetal maturity, to too long a test of labor, to efforts of operative delivery through the pelvis, and occasionally to congenital fetal anomalies. Cesarean section gives no assurance of delivery of a living baby, but, on the other hand, it should not be charged with the responsibility of fetal death, and, too, many a baby has been saved through its use which otherwise would have been lost.

DANIEL G. MORTON, M.D.

Smith, W., and Wilson A.: Effect of Gorse Extracts on the Uterus. *Brit. M. J.*, 1943, 2: 322.

In parts of Yorkshire and Derbyshire infusion of gorse is a traditional remedy for retained placenta in the cow. An apparently successful demonstration of its efficacy aroused the authors' curiosity and led them to test its effect upon isolated strips of the guinea-pig uterus. Sustained tonic contraction was consistently produced by the addition of the watery extract to the fluid in which the uterus was suspended. The consequent investigation was designed to isolate the active principle and to determine its chief pharmacological actions.

Attempts to isolate the active principle have so far been unsuccessful. Preliminary investigation indicates that ulex gallii contains at least one active principle with pharmacological activity, chiefly on the uterus, in several species, and thus affords some rational basis for its empirical use in farmyard obstetrics. The definite effects of extracts upon the isolated human uterus suggest a possible extension to human obstetrics, but further work on chemical fractionation and purification is desirable before clinical tests are made, because there are some indications that the extracts thus far obtained may contain more than one pharmacologically active substance. There is no present indication that the active substance is an alkaloid, but its extraction with ether from alkaline aqueous solution suggests that it is a base, the acidity of the extract being due to a weak organic acid present as an impurity.

The mode of action of the extract remains to be elucidated. Atropine does not affect the reactivity of either the guinea-pig or pregnant human uterus, and the response of the human uterus to adrenaline is not influenced by the extract. The relaxation effect on parturient guinea-pig and nonpregnant human uteri invalidates comparisons with pituitary extract.

The increased sensitivity of uteri from guinea pigs in estrus and the altered reactivity of uteri from parturient guinea pigs and from women near full term are of special interest; they suggest that the effects of the administration of gorse extract may be largely determined by the balance of gonadotropic hormones, which widens the field of possible clinical application. The advantages of a common plant as the source of an oxytocic drug are obvious, provided a satisfactory method of extraction becomes available.

CHARLES BARON, M.D.

GENITOURINARY SURGERY

ADRENAL, KIDNEY, AND URETER

Gilligan, D. R., Garb, S., Wheeler, C., and Plummer, N.: Adjuvant Alkali Therapy in the Prevention of Renal Complications from Sulfadiazine. *J. Am. M. Ass.*, 1943, 122: 1160.

While toxic reactions from sulfadiazine therapy are fewer than are such reactions from other sulfonamides, the frequency of renal complications demands attention. Such reactions vary from microscopic hematuria, ureteral colic, or abdominal pain, to gross hematuria, oliguria, or even anuria with azotemia. Ureteral catheterization and lavage have been necessary at times to remove concretions, and several deaths have been reported from anuria.

Since the renal complications of sulfadiazine are generally, if not always, due to the precipitation of some form of the drug within the kidney or urinary tract, it seemed that a means of preventing this "chemical" toxic effect might be found. Since the renal complications comprise more than one-half of the toxic reactions due to sulfadiazine, the safety of therapy would be much enhanced by the prevention of this effect.

The urinary precipitate which causes renal complications and obstruction to the urinary flow during oral sulfadiazine therapy usually consists chiefly of acetylsulfadiazine. Free sulfadiazine sometimes precipitates in the urine after the intravenous use of sodium sulfadiazine.

The urine is almost always acid, usually with a *p*H of from 5.0 to 6.0, in patients receiving sulfadiazine without adjuvant alkali therapy. With minor exceptions, crystalluria from sulfadiazine is found only in acid urines. The solubilities of sulfadiazine and of acetylsulfadiazine in buffers and in urine increase a great deal with increase of the *p*H within the physiological range of the urinary *p*H. The amounts of sulfadiazine and of acetylsulfadiazine dissolved in a given volume of buffer solution or normal urine at *p*H 7.5 are approximately twenty and thirty times, respectively, the amounts dissolved at *p*H 5.0.

Crystalluria and evidence of renal damage or of urinary-tract obstruction were not encountered in 350 patients in whom the urine was maintained neutral or alkaline by adjuvant alkali therapy during treatment with 6 gm. of sulfadiazine daily, or in smaller groups of patients receiving twice this dosage of sulfadiazine orally, or sodium sulfadiazine intravenously.

Based on clinical studies, the administration of 15.6 gm. daily of sodium bicarbonate, or amounts of other organic sodium salts with equivalent available base excess, divided into six doses of 2.6 gm. (40 gr.) every four hours, is recommended as the dosage that is usually appropriate to maintain the urine neutral or slightly alkaline during sulfadiazine therapy in adults. For patients receiving unusually large doses of the drugs, suitable alkali-therapy regimens have been adopted. A sufficient volume of fluid should be given to provide a daily urinary output of 1,500 cc., or more.

The findings of these laboratory and clinical studies lead to the conclusion that renal damage and urinary-tract obstruction consequent to precipitation of sulfadiazine and acetylsulfadiazine are preventable, and that adjuvant alkali therapy sufficient to maintain the urine neutral or slightly alkaline should be prescribed whenever sulfadiazine is administered.

ARTHUR H. MILBERT, M.D.

Sharp, R. F.: Evaluating the Ureteral Splint. *South. M. J.*, 1943, 36: 549.

The use of some kind of a splinting catheter in the ureter has been a routine procedure with most men performing plastic operations on the renal pelvis or ureter. A report is made on 13 cases operated upon during the past seventeen months. In 10 instances in which a ureteral splint was utilized, excellent results were obtained, while in 3 cases in which a splint was not used the results were poor. Seven of the cases are presented briefly.

Questionnaires received by the author from 6 prominent urologists in the country revealed a decided trend toward the use of some form of ureteral splint. Plastic operation on the ureteropelvic segment was a unanimous indication, with repair of ureteral injuries, a second indication. Correction of tortuosity of the ureter and use of the ureter following the removal of calculi from the kidney and ureter were other indications given.

The splint may be introduced cystoscopically in the form of a ureteral catheter; through the pyelotomy incision and down the ureter, with the upper end extending out through the wound; and, finally, by the most popular method, as in nephrostomy-ureteral drainage. As to the type of splint used, a soft rubber catheter is preferred, with a warning that it not be too large. For dilatation of a constricted ureter, catheters of appropriate size must be used. The size range is from 7F to 14F. A self-retaining nephrostomy catheter with ureteral splint added to it has been devised, together with additional provision for two-way irrigation.

The duration of the splinting depends upon the type of operation and the amount of infection present. The recommended time varies from three days to three months. To prevent kinking of a tortuous ureter when not severely infected, from three to four days will suffice. When marked adhesions are encountered or severe infection is present, from one to three weeks is the customary time. In the plastic operations on the pelvis prolonged splinting up to three months is sometimes indicated.

ARTHUR H. MILBERT, M.D.

BLADDER, URETHRA, AND PENIS

Potter, S. B., and Low, H. T.: Gynecological and Urological Management of Cystocele. *J. Urol.*, Balt., 1943, 50: 322.

The subject of cystocele, or vesical herniation, is discussed from an anatomical and physiological basis. The significant literature is reviewed briefly and 317 cases are presented which were seen during a four-year period, from 1937 to 1941. The part played in this series by the urologist was three-fold: (1) he made the preoperative diagnosis and determined the urinary-tract pathology and therapy; (2) he suggested the necessary operative treatment; and (3) he had charge of the postoperative urinary-tract care.

In this series of cases it was necessary to carry out a combined abdominoperineal procedure in 150 instances because of complicating circumstances of pelvic pathology. In 60 individuals perineal repair was adequate. Vaginal hysterectomy was employed 27 times and only in complete procidentia. Sixty-four abdominal hysterectomies were found to be necessary, primarily to cope with uterine neoplasm, and in these cases the cystocele was a secondary consideration.

With respect to postoperative urinary-tract complications there were noted 38 instances, or 12 per cent. The severity varied, but therapy was not required for more than three months. In 23 instances of the 38, additional hospitalization was necessary. There was knowledge of but a single recurrence, and the mortality in the series was 0.6 per cent. It is pointed out that this series of cases demonstrated to the authors that close co-operation of the gynecological and urological departments led to greatly improved surgical results. Several roentgenographic illustrations and two sketches to emphasize the anatomical considerations in the surgical repair of a cystocele are included in the article.

ROBERT LICH, JR., M.D.

Herger, C. C., and Sauer, H. R.: A Consideration of the Response of Bladder Tumors to External Radiation. *J. Urol.*, Balt., 1943, 50: 310.

The subject of external radiation therapy with regard to carcinoma of the bladder is discussed and 160 cases treated during a three-year period are presented. Success or failure in this therapy is discussed with reference to such factors as: histology, size, tumor extension, general physical condition of the individual, radiosensitivity of the neoplasm, technique of radiation, and amount of radiation energy employed. Tumors were divided into radiosensitive (tumors responding favorably to radiation of less than 2,500 roentgens), radioresponsive (tumors responding to from 2,501 to 5,000 roentgens), and radioresistant (tumors requiring more than 5,000 roentgens).

The series of patients treated fell into the following groups: papillary carcinomas (25), papillary infiltrating carcinomas (91), and solid infiltrating carcinomas (44). In the first two groups (papillary and papillary infiltrating carcinomas) 50 per cent of the patients demonstrated satisfactory results. In fact, 13 of these tumors disappeared and in 44 instances there was sufficient tumor regression to permit transurethral therapy. In 24 patients the regression of the neoplasm was temporary, and no response was noted in 35.

In the group of solid infiltrating carcinomas only a single instance of success was recorded. This group was considered as being treated more successfully by interstitial radiation and surgery since the lesions were decidedly radioresistant to external roentgen therapy.

The entire subject is discussed in considerable detail and the article is illustrated statistically. Two cases of advanced papillary vesical lesions are briefly presented with roentgenographic reproductions.

ROBERT LICH, JR., M.D.

Priestley, J. T., and Strom, G. W.: Total Cystectomy for Carcinoma of the Bladder. *J. Urol.*, 1943, 50: 210.

In an attempt to evaluate total cystectomy as a method of treatment in certain types of carcinoma of the bladder, a review of all cases in which total cystectomy was contemplated at the Mayo Clinic from 1910 to August 31, 1942, inclusive, has been made. Despite the comparatively high operative mortality rate associated with this procedure in years past, total cystectomy has appeared to be the only hope of cure in many cases of carcinoma of the bladder and has been employed more frequently in recent than in earlier years. Indications for the operation remain controversial and will be determined definitely only by more experience. Careful selection of patients and close attention to preoperative and postoperative care as well as to the fundamentals of operative technique have reduced the initial operative mortality rate to a point where total cystectomy can be considered a justifiable procedure. These various aspects of the subject are discussed. Determination of ultimate survival rates must await the lapse of more time.

GENITAL ORGANS

Viethen, H.: The Problem of Early Diagnosis of Carcinoma of Prostate (Das Problem der Fruehdiagnose des Prostatakarzinoms). *Zschr. Urol.*, 1942, 36: 310.

Of 40 patients operated on by the author within the last nine months for hypertrophy of the prostatic gland, 7 or 17.5 per cent, had a cancer. Perineal prostatectomy was performed in each instance and serial sections of the removed glands were made.

The speed with which local recurrences appear, seems to increase with the size of the primary tumor.

Early diagnosis is of paramount importance and should be based on the general examination, x-ray studies of the osseous system, rectal examination, and endovesical and cystographic studies, supple-

mented by biopsy. As to the last procedure, various approaches to the prostatic gland have been used: (1) through the urethra, (2) through the bladder after suprapubic cystostomy, (3) through the perineum, and (4) through the anterior wall of the rectum.

The author advocates the last mentioned, the so-called transrectal biopsy, which is of relatively recent origin and appears harmless. Infections, hemorrhages, and the formation of metastases or of fistulas are the potential dangers but according to the literature they have not yet been observed. The author constructed a 16 cm. long instrument resembling a trocar, which is introduced into the prostatic gland through a rectal speculum under spinal anesthesia. After the tip of the instrument enters the gland, the occluding mandrin is withdrawn and replaced by a stylus which carries a knob on its end. The edge of the knob pointing toward the handle of the carrier is sharp so that some tissue is cut away when the carrier is withdrawn. This instrument was used successfully in 12 cases. JOSEPH K. NARAT, M.D.

MISCELLANEOUS

Kenny, G. E., Cohen, S. E., and Bauer, L.: Preclinical Genitourinary Tuberculosis. *Am. J. M. Sc.*, 1943, 206: 204.

The authors point out that tuberculosis does not particularly respect the classification of Ranke in reference to sequence; that is, it does not follow automatically from stage I to II to III but may proceed directly from I to III and then to II. Hence, with this in mind it can be seen that it is possible for frequent disseminations to occur. In the way of explanation: stage I is the primary focus, stage III is organ tuberculosis, and stage II is dissemination.

The urinalysis offers the most important means of determining the presence of genitourinary tuberculosis. The normal male urine may contain, after centrifugation, 6 pus cells per high-power field in 15 cc., and in the case of the female, 15 cells. In the presence of tuberculosis the urine may show albumin, red cells, or an increase in the number of pus cells; hence, any variation from the normal suggests the immediate need of a twenty-four-hour urine examination with the study of a smear, along with a culture and animal innoculation. Such twenty-four-hour urine examinations are to be repeated at biweekly or monthly intervals until the urologist has sufficient data to outline his plan of cystoscopic and pyelographic examinations. This is the plan of investigation followed at the Municipal Sanatorium at Otisville, New York, which receives the cases of pulmonary tuberculosis from the clinics and hospitals of the City of New York.

During the interval from August, 1940 to February, 1942, 1,230 individuals were treated at this sanatorium. Of this group 214 individuals were studied by means of a total of 393 twenty-four-hour urine specimens. The tubercle bacillus was isolated in 29 instances, representing 14 individuals, and the incidence of genitourinary tuberculosis in the whole group was 1.2 per cent. Since one individual presented clinical evidence of tuberculous orchitis, this study revealed 15 cases, or a 7 per cent incidence, of genitourinary tuberculosis in this group who were subjected to careful urine studies. All organisms isolated were studied culturally and by animal inoculation. One was found to be a smegma organism.

The cases were divided into three separate groups:

1. Clinical genitourinary tuberculosis. Two cases in this group demonstrated marked clinical evidence of genitourinary tuberculosis. The organisms in the twenty-four-hour urine specimens were abundant.

2. Subclinical genitourinary tuberculosis. In this group the symptoms and complaints were vague or absent. However, an abnormal urine suggested twenty-four-hour specimens which revealed successive positive smears or cultures. This group differs from the first only in extent of the process.

3. Tuberculous bacilluria, occult genitourinary tuberculosis. The excretion of tubercle bacilli was inconstant and no definite lesion was revealed. These cases could then go on to the ulcerative stage or proceed to healing as is the case with other foci, such as in the lungs.

The authors note that genitourinary tuberculosis complicates pulmonary tuberculosis more often than is generally thought. Also, that genitourinary tuberculosis is not diagnosed early since it is asymptomatic. In reference to dissemination, genitourinary tuberculosis is spread by the hematogenous route so that a bilateral infection results in the renal cortex. The lesion may then either heal spontaneously or extend to the calyx by passing through the medulla and producing a clinically demonstrable renal lesion. It is also emphasized that tuberculosis in any organ can erode into the blood stream and thus produce excretory tuberculosis even in the tertiary phase of Ranke.

In reference to the contention that the tubercle bacillus may pass through an uninfected kidney, the authors present the work of Medlar and Sasano who showed in guinea pigs that those that excreted bacilli in the urine demonstrated a renal lesion on necropsy. This was further substantiated by Spitzer and Williams, and Munro and Bond.

Morse and Scott examined the urine of patients with pulmonary tuberculosis and found a 3.8 per cent incidence of bacilluria. In support of healing in renal tuberculosis the work of Beach and Schultz is mentioned; these workers studied 8 patients who demonstrated bacilluria and followed them up for from eight to fifteen years. Since there was no recurrence of the bacilluria and the individuals remained asymptomatic it seemed evident that the renal lesions were healed. ROBERT LICH, JR., M.D.

Jones, N., and Warren, S. L.: The Concurrent Use of Sulfathiazole and Hot Baths in the Treatment of the Sulfathiazole-Resistant Case of Gonococcal Infection. *Am. J. Syph.*, 1943, 27: 572.

Sulfathiazole-fast gonorrheal infections are quite common, and this fact is important in the solving of

venereal-disease problems in the organization and mobilization of an armed force approaching ten million men and women, and in the concentration of large numbers of workers in large industrial centers. Before sulfadiazine and sulfathiazole were used, fever therapy alone cured 87 patients in a group of 100 cases, while 64 patients who failed to be cured by one or more courses of sulfanilamide therapy were treated by a single fifteen-hour fever at 41.5°C. with only 1 failure. It has been shown that fever therapy speeds up the chemical reaction or the beneficial effect of chemotherapy when one or the other does not seem to be efficacious.

Since June 15, 1942, 17 patients representing so-called sulfathiazole failures have had negative cultures and smears after a single five-hour fever at 41.1°C. In these cases the sulfathiazole had been terminated from two to ten days previous to the fever therapy. Unfortunately, these cases have not been followed for three months and it is impossible to state that they have been cured. It has been observed that the previous administration of sulfanilamide or sulfathiazole, even though not curative, seems to make the gonococcal infection more susceptible to a short fever treatment, and there seems to be good evidence of a summation of the effects of a sulfonamide and fever when used concurrently.

An empirical schedule may be set up for the treatment of gonococcal cases which are refractory to sulfathiazole treatment alone. There is much clinical evidence to show that these cases are more susceptible to elevated body temperature than usual. A hot bath and concurrent sulfathiazole treatment combines the effects of both an elevated body temperature and a drug, so that each may enhance the effect of the other. Such a routine, during which the blood levels of the sulfathiazole are at their peak, should cure a certain percentage of sulfathiazole-resistant cases of gonococcal infection. This is a practical procedure and can be worked out in such a manner that the majority of the sulfathiazole-fast cases may be cured. ELMER HESS, M.D.

Noojin, R. O., Callaway, J. L., and Schulze, W.: Sulfadiazine and Sulfathiazole Therapy in Lymphogranuloma Venereum and Chancroid. *Am. J. Syph.*, 1943, 27: 601.

Ten patients with lymphogranuloma venereum, 10 patients with chancroid, and 10 patients with lymphogranuloma venereum and/or chancroid were treated with sulfadiazine and sulfathiazole equally. This study was carried out to compare the efficacy of sulfadiazine with that of sulfathiazole in the treatment of these two conditions.

The diagnosis of lymphogranuloma venereum was established by a positive Frei test. The diagnosis of chancroid was established with a positive intradermal reaction to Ducrey vaccine plus the identification of the Ducrey bacillus on smears made from the genital lesions of 8 patients. Group 3 reacted positively to the Frei test as well as to the Ducrey vaccine.

Half of each group were given sulfadiazine and half were given sulfathiazole. The first day each patient received 6 gm. of the drug and for twenty days thereafter he received 3 gm. daily. Blood levels were taken, and the concentration levels were generally less for the patients taking sulfathiazole than were those for the sulfadiazine group. One patient developed drug fever.

Regardless of which drug the patients were treated with, 28 of 30 reported that after institution of the therapy they felt better.

In all of the patients the Frei and Ducrey tests were unaltered at the end of the treatment period, and they were unchanged in 11 patients seen six months later.

It is believed that the exhibition of both of these drugs prevented lymph-node suppuration and drainage when these two processes had not already occurred.

Sulfadiazine is recommended as the drug of choice because it does not produce the drug reactions that are more common when sulfathiazole is used.

ELMER HESS, M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS

CONDITIONS OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Robertson, D. E.: The Medical Treatment of Hematogenous Osteomyelitis. *Ann. Surg.*, 1943, 118: 318.

Hematogenous osteomyelitis in childhood and adolescence and, infrequently, in adult life, is mainly due to the staphylococcus or the streptococcus. The staphylococcus caused over 90 per cent of all cases in this and other series. The organism gains entrance to the blood stream through lesions of the skin, of the mucous membrane, or of the tonsils. The blood becomes contaminated and the organisms are deposited in certain areas of the body. It has been shown experimentally that viscera, muscles, and bones may develop abscesses. In bone the areas involved are the epiphysis, the metaphysis, and the periosteum. There has been much work done to explain the occurrence of abscesses at these situations. A study of the autopsy records of patients dying of this disease shows the same distribution of abscesses as in the experimental animals dying of it.

In view of these findings it is strange to think of osteomyelitis as a local surgical condition, and it is, therefore, rational to look for an agent that will assist in preventing this appalling chain of full-blown septicemia. The mortality records prior to the administration of sulfonamides was about 22 per cent in the author's series. The author strongly suspects that so-called undiagnosed and untreated cases would show no such mortality as 20 per cent.

What are the methods used by nature to subdue this invasion? Ninety per cent of the deaths in the past have occurred in the first and second weeks. The natural antitoxin developed as a reaction to toxin is useful in dealing with the toxin elaborated, but has no effect on the extermination of the invader. The human organism, kept from being overwhelmed with poison, is capable of producing and maintaining agents, phagocytes and bacteriolysin, that directly attack and destroy the invader. While this conflict is progressing, the patient afflicted has all the signs of a reaction, and until the balance is well in favor of the defense, that reaction is very obvious, both generally and locally. From then on there is no real reason that the defense should not greatly increase its power so that the general invasion is wholly under control. The whole system of defense is apparently predicated upon the extermination of the invader, or at least containing him until protective substances can be developed and he can be brought under control.

It is now well established that the sulfonamide drugs are capable of effecting a condition in the blood that will inhibit the growth of organisms. We should, therefore, test the possibilities of these drugs as an aid in treatment. It would seem rational to attempt to introduce into the blood, at the earliest possible moment, a sufficient quantity to render innocuous, or impotent, organisms that are in the blood stream or in reach of body fluids. In the case of the staphylococcus, particularly, which operates by means of a toxin high in necrotizing qualities and the production of thrombosis, it is urgent to administer the drug at the earliest possible moment and in quantities sufficient to the need. How great the need may be can be determined accurately only after the event, so that the assumption of the need is all that is required for the heavy administration of the drug. It is the author's practice to give children of about eight years of age from 8 to 10 gm. daily. They are thus able to maintain levels of from 6 to 12 mgm. per cent in the blood. Larger doses may be possible, even desirable, but at this level there have been a number of reactions. The relation between the drug administered and the concentration in the blood varies greatly in different individuals. Some, when given 10 gm. of sulfathiazole will be found to have a blood level of 4 mgm. per cent only, while the quantities may be entirely different in other cases. For instance, one patient was given 6 gm. of sulfathiazole daily for sixteen days, and her blood level never went higher than 3 mgm. per cent. She then had a reaction, and had no drug for two and one-half days. She was then given 6 gm. of sulfadiazine daily, and the blood level rose to 11.9 mgm. per cent.

It has been proved that pathogenic organisms can become drug-resistant, and this probably happens with the staphylococcus and streptococcus. This would lead to the use of large doses while the organism is still vulnerable. Reactions to the drug in use may make it necessary to discontinue its administration. Thus, when a patient who is having sulfathiazole administered shows signs of a rash, high temperature, nausea, or blood in the urine, this drug is discontinued for a few days and then sulfadiazine is given. It has been found that this may then be borne for the remainder of the period desired. The use of initial large doses is so urgent that one is not justified in testing out the patient to estimate his ability to tolerate the drug. There is apparently no evidence available to the effect that patients who do not tolerate the drug without reaction are not benefited from its action. Sulfonamides do not inhibit the antigenic power of the toxin.

Reports of cases treated by use of the drug, with no incision of the lesion in bone, have been reported by Hoyt et al. They report no deaths in their 12 cases. These cases were all due to the staphylococcus. This series constitutes a unique record, and must give thoughtful surgeons reason to reassess the whole problem of the treatment of acute osteomyelitis. If patients will survive spontaneously, on

the one hand, and if 12 consecutive patients will survive the acute phase with medication with sulfonamides, the part played by surgical incision of the local lesion is certainly not a factor in saving life.

The author's records of 89 cases, (3 moribund on admission) show, since sulfonamide administration, 25 patients not operated upon with 1 death and the others operated upon with 1 death; this is a total mortality rate of 1.2 per cent, excluding the moribund case on admission. These results are not such that, from the mortality standpoint, incision can be altogether condemned when added to sulfonamide medication.

In the subsidence of the acute phase a dramatic change takes place. It occurs over a period of from ten to twelve hours. The general reaction of the patient subsides; the intense swelling of the soft tissue at the local lesion diminishes; the underlying abscess becomes more obvious in its outline; and the patient is comparatively comfortable. Later, the abscess may increase or diminish in size. When it subsides it may, in the course of three or four weeks, entirely disappear. In conditions in which it becomes more superficial and enlarged it may so involve the skin that it opens spontaneously through a small opening. In the author's experience with a case in which a sinus of this type was formed, there was no large sequestrum present in the underlying bone. There were, however, small areas in the bone lined with granulation tissue and containing very small, fragile sequestra. Mostly, the cavities were subperiosteal and contained granulation tissue only. It seems that unless the abscess is very superficial it will not drain of itself, but will tend to subside and behave in every particular like a tuberculous abscess. Any dead bone within it may be disposed of by the action of the tissues and their fluids, or it may become regenerated. It may be said that a sequestrum may be dealt with spontaneously unless a sinus develops or be made, in which circumstance it will be necessary to remove it before the sinus will heal. The pathological change in bone, as evidenced roentgenologically, is different from that in cases in which the lesions are drained. In drained lesions there is generally a wide destruction of bone together with a large involucrum; sequestration is present in over half of the cases. The first change that can be recognized in bone of undrained cases occurs in about eight or ten days. From then on the lesion continues to lose density, and an involucrum very much diminished in extent, sometimes hardly present, may be seen. There is no obvious death of a large mass of bone, except in rare cases, and sequestration is present in only about 10 or 15 per cent of the cases. Secondary lesions in other bones are rare, and when they occur, their course is very much attenuated, and a nonvirulent process with mild pathological changes is found.

The cases treated in this series had ordinary supportive treatment, together with sulfonamides. The author used sulfathiazole, but he believes that sulfadiazine is more readily borne, can be given over a longer period of time, and maintains a higher blood level. It may be a better drug for the treatment of osteomyelitis. He used no splinting except when a joint was involved, then traction was sometimes employed.

An early recognition of the true character of the disease from the history and the general and local symptoms is essential to adequate medication. There is reason to believe that the administration of sulfonamides in heavy doses early in the disease may prevent deaths occurring from this disease. The medication must be adequate, that is, large doses must be given early. Incisional interference is not a factor in saving lives, and may be a very deleterious proceeding. ROBERT P. MONTGOMERY, M.D.

Kehl, K. C.: Dupuytren's Contracture as a Sequel to Coronary Artery Disease and Myocardial Infarction. *Ann. Int. M.*, 1943, 19: 213.

The changes in the palmar fasciae, closely resembling Dupuytren's contractures, and coronary vascular accidents bear a definite relation to each other. Changes in the palms have not been noted in any instance before the onset of the cardiac difficulty. The coronary occlusion, therefore, apparently acts in some obscure manner as the precipitating factor. In the cases presented, Dupuytren's contracture appears to be a complication of or a sequel to coronary occlusion, as well as the shoulder disability described by several authors, and the hand syndrome as noted by Askey.

The palmar changes, as noted in the cases presented, appear typical of Dupuytren's contracture. The typical course is slow but continuous and in the advanced stage results in permanent flexion of one or more fingers to a variable degree.

Six cases of Dupuytren's contracture as a sequel of coronary occlusion are presented. Dupuytren's contracture may be associated with the syndrome of shoulder disability and painful hands following myocardial infarction. Pain, stiffness, swelling, livid discoloration, numbness, tingling, and abnormal skin temperature of the hands may be associated with the palmar changes. The etiology and pathogenesis are not understood, but irritation of the sympathetic ganglia may play an important etiological role.

ROBERT P. MONTGOMERY, M.D.

Blackford, L. M.: Hemangioma of the Vertebra with Compression of the Cord: Report of a Case Cured with Radiation Fourteen Years Ago. *J. Am. M. Ass.*, 1943, 123: 144.

A case of hemangioma of the vertebra is reported in detail. The patient was a young man eighteen years of age. Pain had been initiated in the back by a minor incident. Two months later a tumor developed over the 11th dorsal vertebra, associated with excruciating pain which radiated to the right groin when pressure was made over the tumor. Three months after the initial incident the blood pressure was markedly elevated, the back was held rigid, and the tumor now measured 4 cm. in diameter.

It had the external appearance of a mass of tangled veins. Neither pulsation nor bruit was observed. Hyperesthesia and sensory changes were noted. Some reflexes were pathological.

A roentgenogram of the spine did not aid in the diagnosis. Aspiration revealed blood. The Queckenstedt test showed a complete block.

The patient was operated upon three months from date of the initial symptoms. Tremendous hemorrhage was encountered. A biopsy was taken, and the diagnosis was osteogenic sarcoma. Roentgenotherapy was administered on three occasions. Similar roentgenotherapy was again administered at four months in three doses. Six months after the initial symptoms occurred the pathological neurological signs had cleared up.

After one year the sensory changes had entirely disappeared and the blood pressure had returned to normal. Thirteen years following the operation the patient was awarded a commission in the Armed Forces and he is now in active service.

The pathologist reviewed the histological sections and made a final diagnosis of hemangioma of the vertebra. The author believes that surgery should not be attempted in cases of this type until roentgenotherapy has failed or until paraplegia occurs.

Sixty-five similar cases have been investigated. Surgical attack has carried a high mortality.

RICHARD J. BENNETT, JR., M.D.

SURGERY OF THE BONES, JOINTS, MUSCLES, TENDONS, ETC.

Armstrong, J. R.: Bone-Grafting in the Treatment of Fractured Tibia and Fibula. *Lancet*, 1943, 245: 188.

Treatment of a fractured tibia and fibula by open operation is rarely necessary, particularly if adequate conservative methods are employed from the outset. It must be emphasized that although the penalty of failure of conservative treatment may be heavy, the result of failure of operative treatment may well be tragedy. There are four absolute indications and two relative indications for operation. The absolute indications are: (1) established nonunion, (2) malunion sufficient to cause serious disability, (3) failure to obtain adequate reduction by conservative methods, and (4) loss of bone sufficient to prevent union or to delay it unduly. The two relative indications for operation are: (1) delayed union in certain circumstances (in some of these fractures it may be justifiable to hasten union by bone-grafting), and (2) grossly unstable fractures, such as notably very oblique fractures with a loose "butterfly" fragment, in which it may be impossible to maintain accurate reduction by conservative methods alone.

There are two contraindications to operation. The first is local infection in the affected limb, either of the skin, bone, or other tissues, or an active septic focus elsewhere in the body; fractures in which there has been an infection of bone should be approached with special care, because very often an apparently subsided focus will "flare" after an operation. The second contraindication is any doubt at all of the absolute efficacy of the theater technique available. Unless the aseptic technique is completely reliable, operation is unjustifiable.

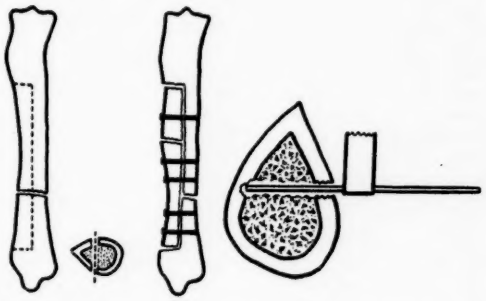

Fig. 1. a, How a massive sliding graft is cut. b, The massive sliding graft in place. c, Cutting the graft. Division of one cortex and part of the other.

Three essential results should follow an ideal operation: (1) restoration of the normal relationship between the bony fragments; (2) mechanically stable fixation of the fragments in normal relationship; and (3) the establishment of conditions most favorable for subsequent union of the bone. Many types of operation fall short of these requirements.

Simple reduction after "freshening" or drilling of bone ends is not mechanically stable, and displacement may recur. Reduction and fixation with screws or plates of vitallium or other material does not produce conditions as favorable for union as those obtained with procedures using autogenous bone grafts. With autogenous grafts it is difficult to produce stable fixation by relying only on accurate fitting of the graft. The introduction of nonionizable metals, such as vitallium, has made it possible to combine the best features of these procedures by using massive grafts of autogenous bone fixed by screws. In this way a very stable fixation is produced; there is no danger of the screws working loose because of bone absorption, or adversely affecting the process of bony union, and no fear of subsequent ill effects due to the presence of an ionizable metal in the tissues.

The author has found the use of a massive sliding graft consisting of half the tibia, on the principle described by Gill (1932) in connection with the radius and ulna, an improvement over either inlay or outlay grafts. The tibia is exposed subperiosteally along its whole length, the fracture is reduced and held so that the fragments are in normal relationship, and the bone is split in two along about half its length in such a way that two-thirds of the divided area is on the longer, and one-third on the shorter, fragment. The bone is divided approximately at its center and the anterior fragments are removed (Fig.

1a). The longer fragment is laid across the fracture and fixed in position with vitallium screws, and the gap left is filled with the shorter fragment (Fig. 1b). The fibula is next refractured or, if necessary, divided subperiosteally. This is a most important step if the presence of an intact fibula prevents accurate alignment of the tibial fragments. With a large diameter single saw the bone is split as shown in Fig. 1a. If a saw 1¾ in. in diameter is used it is possible to divide one cortex, cross the medullary cavity, and partly divide the opposite cortex with a single cut (Fig. 1c). If a larger blade is available the bone can be completely divided. The longitudinal cut is made first, care being taken to keep parallel to the posterior surface of the tibia. The leg is covered with a sterile towel and anteroposterior and lateral roentgenograms are taken to confirm satisfactory alignment of the tibial fragments.

If a padded plaster cast is used it should be replaced by an unpadded plaster two weeks after operation, leg-raising exercises being omitted until after this has been done. An unpadded plaster need not be changed for six weeks after operation. The patient is allowed to sit up in a chair two weeks after operation and to begin walking on crutches from two to three weeks later. Full weight-bearing in plaster is not permitted for at least six weeks after operation.

ROBERT P. MONTGOMERY, M.D.

FRACTURES AND DISLOCATIONS

Hartley, J. B.: "Stress" or "Fatigue" Fractures of Bone. *Brit. J. Radiol.*, 1943, 16: 255.

In a most beautifully illustrated and composed paper the author discusses "fatigue" fractures. A stress, insufficiency, or fatigue fracture is a condition occurring in apparently normal bone and is demonstrable roentgenologically as a partial or complete line running transversally to the axis of a long bone. The roentgenogram shows either a "submicroscopic or molecular" fracture enveloped by callus formation or a more distinct line is found in subsequent radiological pictures. A fatigue fracture may reveal itself by the clinical course of the condition.

Fatigue fractures have to be differentiated from: (a) spontaneous fractures, i.e., spontaneous fractures through pathological bone; (b) from pseudofractures showing "Umbauzonen," i.e., Loosers transformation zones; and (c) from pathological fractures, a self-explanatory term.

Fatigue fractures occur most frequently in adolescence, between the ages of seven to twenty years. In most instances weight-bearing bones are affected, and the metatarsals, upper third of the tibia, the femur, and the fibula are affected in the order mentioned. The incidence of fatigue fractures (except march fractures affecting the metatarsals) is very low (15) in American and English literature compared with a single report of a German worker who described 590 different types of fatigue fractures.

Features of fatigue fractures in contrast to pseudofractures are presented in table form. In fatigue fractures local pain is experienced during and after exercise, never at rest. There may be local edema. Never is there, however, increased local or body temperature. Callus formation and a definite fracture line can be demonstrated about three weeks after the onset of local pain. The callus formation increases rapidly and shows normal behavior. The site of pathology shows an ill-defined, easily missed, hairline fissure which usually does not extend across the whole thickness of bone. It usually is found on the concave portion of the long bone, i.e., the area of stress. No systemic disease is found. In pseudofractures characterized by "Umbauzonen" the pain has no direct relationship to exercise. Callus formation is usually absent. If any callus is found it remains static for weeks or months and responds only to the treatment of the underlying systemic disease. The fracture is a rather broad, clear-cut line which usually extends across the bone. The site of the fracture line is almost invariably on the convex surface of the long bone, i.e., the stretched aspect.

Several causes have been named as being responsible for the development of fatigue fractures. Nutritional deficiency, polyhypovitaminosis, and weakness of one portion of the bone due to the nutritional foramen are only a few of the advanced theories. The author supports the contention that disproportion between the required and inherent capacities of bone to bear stress is the main factor in the production of fatigue fractures.

The importance of accurate diagnosis is stressed and several conditions are mentioned which must be differentiated.

1. Pathological fractures in congenital defects, general systemic diseases, metastasis, and bone tumors
2. "Umbauzonen" or pseudofractures in Paget's disease, osteomalacia, and rickets
3. Primary malignant disease of bone, such as sarcoma and Ewing's tumor
4. Osteitis due to tuberculosis, syphilis, and low-grade hematogenous osteoperiostitis
5. Simple fractures due to violence
6. Osteomyelitis

In the early stage of the disease a few days of rest and graduated resumption of weightbearing are required. More severe cases require immobilization in plaster and prolonged rest.

In conclusion the author points out that new methods of observation, i.e., the use of radioactive indicators, will help to establish the true etiology and the physiological and pathological processes in fatigue fractures.

GEORGE I. REISS, M.D.

ORTHOPEDICS IN GENERAL

Cureton, T. K.: The Unfitness of Young Men in Motor Fitness. *J. Am. M. Ass.*, 1943, 123: 69.

A series of 1,000 men students entering the University of Illinois in 1940 were tested on aspects of motor fitness, and in 1941 an additional 3,099 men in the service courses were included. The tests were

standardized as 14 hand exercises in addition to a separate group of swimming tests. These were designed to measure balance, flexibility, agility, strength, power, and endurance. The definitions of the last are carefully explained, as well as the importance of each.

The survey revealed that a large number of young men are failures according to the motor-fitness tests. Apparently, physical-training programs are inadequate, and the addition of social programs, such as dancing, bowling, and archery, have detracted from the physical-fitness training programs. The high trend of accident rates, loss of health after thirty, and prevalent chronic disease may be partly due to the physical unfitness of our young adults.

DANIEL H. LEVINTHAL, M.D.

Moldaver, J.: Physiopathological Aspect of the Disorders of Muscles in Infantile Paralysis. *J. Am. M. Ass.*, 1943, 123: 74.

The highly controversial theories regarding causes of paralysis, pain, spasm, and inco-ordination in poliomyelitis have been investigated by the author with electromyographic equipment to measure chronaxie and action currents. The degree of neuromuscular degeneration was evaluated by chronaxie measurements and it was found that the muscles considered as alienated by Kenny were in total neuromuscular degeneration (true paralysis) and not merely "overstretched" or "alienated." Muscles in spasm generally showed normal chronaxie, that is, a normal neuromuscular condition. Forty-nine patients were thus examined.

Sixteen patients were examined with action potentials of muscles in spasm. Spasm was also pronounced in a patient who had only the meningeal signs of poliomyelitis. The more advanced the neuromuscular degeneration, the less was the spasm recorded. Muscle spasm cannot therefore be responsible for the degeneration and paralysis in poliomyelitis.

The author has also presented excellent explanations for the spasm and inco-ordination found in poliomyelitis without embarking on theories lacking a scientific basis. DANIEL H. LEVINTHAL, M.D.

Hershey, C. D.: The Sacroiliac Joint and Pain of Sciatic Radiation. *J. Am. M. Ass.*, 1943, 122: 983.

In the present study the anterior sacroiliac regions of 64 embalmed bodies were dissected. The relationship of the lumbosacral trunk to the sacroiliac joint was determined in all specimens and the degree of arthritic lipping of the joint was noted and classified as to severity. In all specimens the lumbosacral trunk crossed the lower one-third of the sacroiliac joint and lay directly on the joint.

It appears significant that 25 per cent of the bodies examined showed well defined lipping of the joint anteriorly. In many of these the joint line was extremely rough and jagged and in most of the cases the lumbosacral trunk was pushed forward and was forced to angulate over this process. Indeed, in at least 2 of the specimens there was an actual groove in the posterior surface of the trunk at the point at which it was in contact with the joint. Sashin suggested that such a process might affect the nerve not only by direct pressure but also by osteophytes which extend into the nerve itself.

CONCLUSIONS

1. The lumbosacral trunk was in direct contact with the sacroiliac joint at the point at which it traverses the joint in its lower one-third in all of the 64 specimens studied.

2. The upper portion of the origin of the pyriformis muscle was found to lie medial to the lumbosacral trunk in this study and never to lie between the trunk and the joint.

3. Hypertrophic arthritis in the form of severe spur formation on the anterior line of the sacroiliac joint was found to be present in 25 per cent of the bodies that were studied. In most of these this formation was considered capable of having produced direct irritation of the lumbosacral trunk.

4. Hypertrophic sacroiliac arthritis was more frequently found in the older age groups, but it was often encountered in younger persons.

5. Hypertrophic lipping of the joint in its lower one-third where the lumbosacral trunk crosses it can readily be determined by anteroposterior roentgenograms of the pelvis. ROBERT T. MCELVENNY, M.D.

SURGERY OF THE BLOOD AND LYMPH SYSTEMS

BLOOD VESSELS

Lesser, A., and Raider, L.: Venography with Fluoroscopy in Venous Lesions of the Lower Limb. *Radiology*, 1943, 41: 157.

The history of venography is briefly considered, and the technique of the authors is outlined as follows:

The patient is placed prone on the fluoroscopic table with the foot everted and the limb slightly abducted. Under local anesthesia, a vertical incision 1.5 cm. in length is made about 1.0 cm. posteriorly to the external malleolus. At this point a tributary of the short saphenous vein is readily isolated. A No. 19 transfusion cannula is tied in the vein. To this is attached a Luer-Lok syringe containing 30 cm. of 35 per cent diodrast solution. Injection of the opaque medium is then begun under fluoroscopic visualization and is continued while the course and progress of the solution are observed throughout the length of the extremity. This requires from 10 to 15 cc. injected over a period of from ten to thirty seconds, according to the rate of circulation in the limb. Fluoroscopy is then discontinued and a similar amount is again injected over the same time interval, at the end of which x-ray films are made with the patient so positioned as to demonstrate best the area involved.

The important features of the normal venogram are outlined. Five cases in which venography was of value are discussed. The conditions in which this procedure is particularly indicated are: thrombophlebitis, especially with involvement of the deep veins, varicose veins, and arteriovenous aneurysm.

In none of the 25 cases studied were untoward incidences encountered. No thrombi were dislodged and phlebitis did not occur at the site of injection. HAROLD C. OCHSNER, M.D.

Eger, S. A., and Casper, S. L.: The Etiology of Varicose Veins from an Anatomic Aspect, Based on Dissection of 38 Adult Cadavers. *J. Am. M. Ass.*, 1943, 123: 148.

Since it is definitely known that there are no valves in the inferior vena cava and common iliac veins, it is the role of the valves in the external iliac veins to support the column of blood when an individual is in the upright position. Absence of valves in the external iliac veins imposes a greater burden on the valves in the femoral vein. Absence of valves in both the external iliac and femoral veins, above the orifice of the great saphenous vein, imposes an even greater burden of support on the saphenous vein, that is, on the superficial circulation, and results in varicosities.

On an anatomic basis, there is a 36.8 per cent minimal potential incidence of varicose veins in the lower extremities. This potential incidence is further increased by the absence, bilaterally in 36.8 per cent and unilaterally in from 52 to 55 per cent, of the valves in the external iliac veins, with only one valve in each of the femoral veins above the orifice of the internal saphenous vein. These varicosities should develop unilaterally in 28.9 per cent and bilaterally in 7.9 per cent. The left lower extremity should be involved approximately twice as frequently as the right. SAMUEL KAHN, M.D.

Davis, D., Gilman, S., and Freedberg, A. S.: Venous Pressure in the Lower Extremities During Abdominal Operations. *N. England J. M.*, 1943, 229: 272.

Studies of venous pressure in the leg veins during abdominal operations were made in 18 cases. Ten patients had operations on the uterus, 4 underwent cholecystectomy, and 4 were subjected to unilateral herniorrhaphy. The types of operation selected for this study were chosen because the incidence of postoperative thrombophlebitis is different in each.

Appreciable increases in venous pressure in the leg occurred during some stage of all the operations on the uterus. These increases occurred irregularly following the introduction of packs and exploration of the abdominal cavity. Marked rises in venous pressure occurred in almost all of the cases when traction was placed on the uterus or its adnexa, and the pressure generally fell sharply when the traction was released, although it did not always immediately return to previous levels. The application of the dressing and abdominal binder at the end of the operation did not appreciably influence the venous pressure in these cases. In 2 of the 4 patients having a cholecystectomy, the venous pressure showed little change during operation, while it increased in the other 2 patients during operation, but was not increased on application of the binder. In the 4 operations for hernia, the pressure was measured in the veins of the foot on the side of operation. Few changes were noted during operation. In 3 cases the application of the dressing and abdominal binder was accompanied by a persistent increase in venous pressure.

It appears that pressure changes in the leg veins were not related to any general increase in venous pressure and that locally acting phenomena must be considered. Kinking of the iliac vein by traction on the lateral attachments of the broad ligament does not appear to be a likely explanation, since such traction did not appreciably alter the pressure while the uterus and adnexa were in their normal position. Direct pressure on the vena cava, however, could be a factor.

The present study in conjunction with previous studies indicates that local venospasm is a possible factor in the rise in venous pressure during the course of certain operations. However, the duration of the

rise in venous pressure cannot be used as an indication of the duration of the obstruction due to spasm, since the collateral circulation and a general increase in the size of the vascular bed may produce a slow fall in the pressure. The rises in pressure following the application of a binder after herniorrhaphy are probably best explained by mechanical obstruction to the venous return at the anterior rim of the pelvis. The importance of avoiding a tight binder is apparent. JOHN L. LINDQUIST, M.D.

Harrison, P. W., and Chandy, J.: A Subclavian Aneurysm Cured By Cellophane Fibrosis. *Ann. Surg.*, 1943, 118: 478.

It has been shown experimentally that wrapping a blood vessel with ordinary DuPont cellophane has led to a fibrosis which eventually closed off the vessel by contraction. The authors have had opportunity to try out this method in 2 human cases. One of the attempts was successful, while the other eventuated in ligation of the involved artery with an unsatisfactory result. Both of the cases are reported in detail by the author.

It took ten months for the arterial occlusion to progress sufficiently to cause the aneurysm to diminish in size, and nineteen months for the process to be completed. A comparable case was treated by ligation with the result that there was considerable disability in the arm.

The authors are of the opinion that this method of gradual occlusion is valuable and that it might be applied to aneurysms of other arteries, notably the aorta.

The second case, which had an unsuccessful outcome, was complicated by pre-existing skin infection at the site of the wound.

HERBERT F. THURSTON, M.D.

Nicholson, R. E.: The Syndrome of Rupture of an Aortic Aneurysm into the Pulmonary Artery. Review of the Literature with Report of 2 Cases. *Ann. Int. M.*, 1943, 19: 286.

In an extensive review of the literature, the author points out that the incidence of rupture of an aortic aneurysm into the pulmonary artery is rare, and even rarer is the ante-mortem diagnosis of such a condition.

Two cases of rupture of an aortic aneurysm into the pulmonary artery are added to the literature, one occurring in a thirty-nine-year-old female who survived for a period of five months after rupture, and the other in a forty-year-old male whose duration of life following rupture was six days. Both instances were recognized and diagnosed correctly prior to death.

The syndrome of rupture of an aortic aneurysm into the pulmonary artery was accurately described by Hope in his "Diseases of the Heart" in 1839, his conclusions being based on 1 case (Munro's). His description, which was made over one hundred years ago, conforms closely to the concept of the condition as it is understood today.

From a critical analysis of the 81 cases reported in the literature, and the 2 instances occurring at the Charity Hospital of Louisiana, New Orleans, a syndrome of rupture of an aortic aneurysm into the pulmonary artery is formulated:

History. Sudden onset of severe stabbing pain, or a sense of oppression in the precordial area, with or without radiation usually following physical exertion, and succeeded by marked and increasing dyspnea.

Subjective signs. (1) Marked and increasing shortness of breath; (2) progressive swelling of the lower extremities and trunk; (3) rasping cough with expectoration or hemoptysis; and (4) bluish discoloration of the face and extremities (the pallor may be the alternative).

Objective signs. (1) An intense thrill in the second to third left interspace occurring during systole, or continuous throughout the cardiac cycle; (2) a humming "machinelike" murmur, heard best to the left of the sternum in the second or third interspaces, continuous throughout the systolic and diastolic phase and crescendo-decrescendo in character, being more intense during systole (this murmur resembles that heard in a patent ductus Botalli); (3) evidence of aneurysm of the aorta; (4) marked and increasing dyspnea usually reaching the extent of orthopnea; (5) cyanosis of the lips, face, or extremities, or marked pallor of the same areas; (6) edema of the lower extremities and trunk progressing to anasarca; (7) the hemodynamic phenomena of aortic regurgitation (Corrigan's pulse, increased cardiac rate, capillary pulsation, Duroziez's sign); (8) roentgenographic evidence of aneurysmal dilatation of the aorta, prominent and enlarged pulmonary conus, and probable enlargement of the heart; and (9) electrocardiographic indications of a nonspecific character but usually indicative of a sinus tachycardia, right-axis deviation, and lowered, inverted, or diaphasic T-waves in the standard and precordial (IVF) leads.

These findings become even more significant if the patient had been studied previously and was known to have been free of the cardiovascular phenomena described above. JOHN E. KIRKPATRICK, M.D.

BLOOD; TRANSFUSION

Britton, C. J. C.: Serial Leucocyte Counts in Hospital Nurses not Exposed to Radiation. *Lancet*, 1943, 245: 289.

In this hospital 29 per cent of 552 leucocyte counts in 68 apparently healthy nurses not exposed to radiation showed polymorphonuclear or lymphocyte counts below minimum normal levels (viz., below 3,000 polymorphs per c.mm. or 1,500 lymphocytes per c.mm.). There was no significant difference between the figures for nurses on day duty and those for nurses on night duty. This fall in leucocyte count has probably become common since the war began.

A persistently low polymorph or lymphocyte count in a radiation worker does not necessarily mean ex-

posure to radiation. In such case the department should be examined for possible stray radiation, but the person should not be debarred from work unless the polymorph or lymphocyte count falls progressively, as shown by repeated counts at weekly intervals. J. M. MORA, M.D.

Florio, L., Stewart, M., and Mugrage, E. R.: The Effect of Freezing on Erythrocytes. *J. Lab. Clin. M.*, 1943, 28: 1486.

Red blood cells frozen at −75°C. were hemolyzed if stored in the ice chamber of an electric refrigerator. It is probable that temperatures higher than about −40°C. result in a hemolysis of the erythrocytes.

Under experimental conditions described by the authors, it was possible to freeze at −75°C. and thaw human blood with very little destruction of the red blood cells. The speed of freezing and thawing and the addition of 20 per cent glucose were fundamental factors in the preservation of the human erythrocytes by freezing.

By comparison with control specimens of unfrozen blood, it was found that the oxygen-carrying capacity of the frozen blood and the possibility of typing it were not altered by the freezing. The fragility of the frozen and unfrozen cells was the same. ERNEST E. ARNHEIM, M.D.

Shafiroff, B. G. P., Doubilet, H., Barcham, I. S., and Tui, C.: The Coagulability of Venous Blood of Normal and Diseased Legs. *Ann. Surg.*, 1943, 118: 482.

The authors note that in recent years there has been a gradually increasing interest in the differences between the blood of diseased and that of normal extremities. Thus, blood drawn from varicose veins associated with complications has been found, on the basis of comparison with values accepted as normal, to exhibit an increase in viscosity, in the concentration of plasma proteins, in carbon-dioxide combining power, and in the rate of sedimentation. The clotting time, also, has been studied, and has been reported as being "within normal limits." The authors are of the opinion that it is more reliable to use the figures accepted as within normal limits, but to use the clotting time of the blood drawn at the same time from the normal extremity of the same individual. In the following study, this criterion was observed, the venous blood of a normal upper extremity serving as a control. The technique of the procedure used in the study is described.

A study of the coagulation time was made of the blood from the upper and lower extremities of 191 subjects, 28 normal, 156 with varicose veins, and 7 with established thrombophlebitis. It was found that in normal persons there was a slight tendency of the blood of the lower extremity to clot faster than that of the upper extremity.

The authors found that this tendency was moderately exaggerated, in various degrees, by the presence of varicose veins, and markedly exaggerated in the blood from thrombophlebitic extremities. The possible implications of these findings are discussed. In regard to the marked acceleration of clotting of the blood from the veins of extremities with established thrombophlebitis, these questions may be set down:

1. Is this tendency due to the same change as is to be found in blood from varicose veins?
2. Does this tendency antedate the formation of the thrombus?
3. If it antedates the formation of the thrombus may it not be developed into a prognostic test which would indicate preventative therapy before thromboembolization takes place?

Each of the answers to these questions would constitute the definitive result of lines of further investigation. HERBERT F. THURSTON, M.D.

Davidson, C. S., and MacDonald, H.: The Effect of Vitamin K_1 Oxide on Hypoprothrombinemia Induced by Dicoumarol. *N. England J. M.*, 1943, 229: 353.

The authors note that much attention has recently been given to the use of dicoumarol as an anticoagulant. The advantages of the drug over heparin, such as oral activity and relatively low cost, are apparent, but the serious disadvantage of lack of control has been given less attention. It seemed advisable to determine whether vitamin K has any influence on the action of dicoumarol given in therapeutic doses. It is evident that very large doses of the vitamin would be required because usual doses, or even those ordinarily thought to be large, have been shown repeatedly to be ineffective.

The effect of the administration of vitamin K_1 oxide on the hypoprothrombinemia produced by dicoumarol was studied in 5 patients. Two methods of attack were used. In the use of one method, an attempt was made to prevent dicoumarol from having its customary hypoprothrombinemic effect. In the other, the full effect of dicoumarol was permitted to occur and vitamin K_1 oxide was then administered in an attempt to bring the prothrombin concentration back to normal.

In 4 of the 5 patients studied, the administration of vitamin K_1 oxide in large doses either prevented or reversed the hypoprothrombinemia produced by suitable doses of dicoumarol. Just as with the anticoagulant effect of dicoumarol, the amount of vitamin K_1 oxide required to produce an antagonistic effect varies from patient to patient, and repeated doses of the vitamin may be necessary to secure the desired result. The quantitative relation between dicoumarol and vitamin K_1 oxide requires further study. Furthermore, it should be noted that the effect of vitamin K_1 oxide presented in this article is confined exclusively to its effect on the hypoprothrombinemia produced by a single dose of dicoumarol. It will be necessary, therefore, to establish the usefulness of the vitamin as a means of controlling the coagulation time in patients who are receiving a prolonged course of dicoumarol. If, under these circumstances, it can be established that vitamin K_1 oxide acts in a similar fashion to that obtain-

ing for a single dose of dicoumarol, it would seem likely that many of the dangers following the use of the anticoagulant can be removed.

In conclusion, the authors note that the activity of large doses of vitamin K_1 oxide in reversing the hypoprothrombinemia produced by dicoumarol has been demonstrated in 3 of 4 patients studied. It is probable that an inadequate amount of the vitamin was administered to the fourth patient. In 1 patient, the administration of vitamin K_1 oxide prevented the subsequent establishment of a hypoprothrombinemia following the administration of dicoumarol. The amount of vitamin K_1 oxide required to produce the desired effect varied considerably from patient to patient. No serious toxic manifestations were observed from the administration of large amounts of vitamin K_1 oxide. In reversing the hypoprothrombinemia established by single doses of dicoumarol, this anticoagulant may be made safer than it has been heretofore.

HERBERT F. THURSTON, M.D.

Kagan, B. M.: Hyperglobulinemia. *Am. J. M. Sc.*, 1943, 206: 309.

The author notes that almost invariably when the total protein concentration of blood serum is increased above normal, this increase exists because of an increase in the serum globulin concentration. A study of hyperproteinemia is, therefore, essentially a study of hyperglobulinemia. With three major exceptions—(1) all forms of hepatic disease, (2) acute glomerulonephritis, and (3) the simultaneous occurrence of two conditions, the one causing hyperglobulinemia, the other causing hypoalbuminemia—it has been found that whenever the globulin concentration is increased above normal the total protein concentration is usually also increased above normal.

Hyperglobulinemia is considered to exist when the serum globulin concentration is above 3 gm. per 100 cc. or when, in the absence of a globulin determination, the total protein concentration is above 8 gm. Whenever the total protein concentration is above 7½ gm. an abnormal increase in serum globulin is suspected, but it is considered certain only upon actual confirmation of the fact.

The author presents a summary of the data on hyperproteinemia and hyperglobulinemia occurring in dehydration, in diseases involving the bone marrow and in infections. The significance of hyperglobulinemia has been discussed from a clinical and physiological point of view. Hyperglobulinemia appears principally in diseases involving the liver, diseases involving the bone marrow, in chronic infections, and in dehydration.

The accompanying table classifies the cases studied in accordance with the discussion. According to this study and the literature, values for total serum protein concentration over 9 gm. are rarely found except in multiple myeloma, monocytic leucemia, venereal lymphogranuloma, pulmonary suppuration, Boeck's sarcoid, subacute bacterial endocarditis, and dehydration. A few diseases which are rare in this country, such as kala-azar and schistosomiasis, may also produce such changes.

TABLE I.—SUMMARY OF DATA ON HYPERPROTEINEMIA AND HYPERGLOBULINEMIA

	Total protein				Globulin	
	No. cases	No. deter.	No. cases >7.5 gm. per 100 cc.	No. deter. >7.5 gm. per 100 cc.	No. deter.	No. deter. >3 gm. per 100 cc.
Dehydration: Various causes	22	28	17	17	20	15
Diseases involving bone marrow: Monocytic leucemia	1	4	1	4	4	4
Multiple myeloma	2	4	0	0	4	1
Lymphatic leucemia	1	1	1	1	1	1
Infections: Abscess of lung	4	6	4	5	2	2
Bronchiectasis	5	7	4	4	1	1
Chronic pyonephrosis	1	4	1	1	2	2
Chronic osteomyelitis	1	1	0	0	1	1
Boeck's sarcoid	1	1	0	0	1	1
Tuberculosis	12	29	3	4	20	16
Syphilis	12	15	6	6	5	3
Venereal lymphogranuloma	11	11	8	10	8	7
Rheumatoid arthritis	1	1	1	1	1	1
Bacterial endocarditis	7	14	2	6	3	2
Lupus erythematosis disseminatus	2	3	2	2	2	2
Periarteritis nodosa	2	4	0	0	4	4

The presence of an upper threshold of albumin concentration in dehydration is suggested. Increase in the total protein concentration during dehydration in the cases studied was due to an increase in serum globulin, while the serum albumin remained at the upper level of normal or was decreased because of other factors.

The author concludes that the clinical data presented support the theory that serum globulin is formed by the plasma cells and the reticuloendothelial system throughout the body.

HERBERT F. THURSTON, M.D.

Hughes, W. H.: The Blood-Picture after Massive Transfusion. *Lancet*, Lond., 1943, 245: 321.

A fifty-year-old female having group B(III) blood suffered a severe gastrointestinal hemorrhage and was transfused with 4 pints of O blood after cross-matching of each bottle against her serum. The condition being unimproved, more blood was required, and she received altogether 23 pints, 22 of group O and 1 (the ninth) of her own group B. There were two reactions: the first was a typical rigor, which occurred with transfusion of the eighth pint; and a mild reaction and buzzing in the ears occurred

with the twenty-third pint. There was never any jaundice, nor any urinary change.

Examination of the blood one week after the last transfusion showed that the cells still reacted as group B. The serum in the body contained no trace of agglutinins against known corpuscles of all groups; for all practical purposes the patient had become a universal recipient. A week later the alpha agglutinins were again present and they have persisted.

The theoretical aspects of the suppression of agglutinins are discussed. The fact that the agglutinins returned, and that the blood group was not reversed throws doubt on the following two theories: (1) that large transfusions of group O blood into patients of other groups can reverse the blood group, and (2) that transfused serum agglutinins are neutralized by agglutinogens either in the blood cells, the serum, or the fixed tissue cells. The condition observed in this patient may be comparable with the suppression of agglutinins in the fetus.

EDWIN J. PULASKI, M.D.

RETICULOENDOTHELIAL SYSTEM

Lowe, R. C.: A Study of Hemoglobin Metabolism and Hematology in a Case of Congenital Hemolytic Jaundice During (a) Clinical Crisis, (b) Repeated Transfusions, and (c) Before and After Splenectomy. *Am. J. M. Sc.*, 1943, 206: 347.

This case of congenital hemolytic jaundice is reported by the author because of the continuous period of study before splenectomy, through the course of a clinical crisis with evidence of liver dysfunction, during repeated blood transfusions, and, finally, after splenectomy. Although similar studies of hemolytic jaundice before and after splenectomy have appeared in the literature, none covers all of these various phases.

There are several reports of clinical or pathological evidence of liver complications occurring during the course of hemolytic jaundice of various types. The clinical picture includes: (1) liver enlargement; (2) repeated attacks of nausea, vomiting, fever, and progressive jaundice, with upper right quadrant pain in the presence or absence of gall stones; (3) a direct van den Bergh reaction in the serum, or one changing from indirect to direct during the acute episode. The pathological changes observed include: (1) marked enlargement of the liver with no histological reports; (2) a perilobular congestion of characteristic type; (3) some degree of parenchymal degeneration, varying from a mild type with recovery to a severe type with terminal acute yellow atrophy.

The report of this case is given in detail by the author. He notes that the crises of hemolytic jaundice may be characterized by the prominence of various features. They are described as thermic, abdominal, and essential blood crises. During the crisis of the case reported herewith certain observations indicated a decrease of liver function which cleared spontaneously. There was no evidence of marked blood destruction. These changes have been observed also in certain crises of sickle-cell anemia. The findings suggest the theory that liver disease may be a factor in the crises of such cases.

Transfusions were followed by a progressive enlargement of the spleen, and there then occurred a marked increase in blood destruction, a drop in the red blood cells, hemoglobin, and reticulocytes. It is probable that the transfused red cells were sequestered in the spleen and rapidly destroyed, which led to the marked stercobilin excretion.

The author notes that splenectomy was followed by a return to normal of the red blood cells, hemoglobin, reticulocytes, bilirubinemia, and pigment excretion. All clinical symptoms and signs disappeared.

HERBERT F. THURSTON, M.D.

SURGICAL TECHNIQUE

WAR SURGERY

Rowntree, L. G., McGill, K. H., and Edwards, T. I.: Causes of Rejection and the Incidence of Defects Among Eighteen- and Nineteen-Year-Old Selective Service Registrants. *J. Am. M. Ass.*, 1943, 123: 181.

In this article registrants have been counted as rejected if they were not accepted for general military service. However, a substantial number of registrants who were not acceptable for general military service were inducted for limited service. If these men who were accepted for limited service only had been counted as inducted for the purposes of this article, the rejection rates would have been lower, particularly for rejections due to defective vision and musculoskeletal defects.

Of the white youths called up for physical examination, 23.8 per cent were rejected either at local boards or at induction stations. The corresponding rejection rate for negro youths was almost twice as high, 45.5 per cent.

The rejection rates for eighteen- and nineteen-year-old registrants are only slightly lower than the rejection rates for older registrants, but caution should be exercised in drawing conclusions from this since, as noted previously, a large proportion of physically fit youths were not liable for examination either (a) because of previous enlistment in the armed forces, (b) because of programs that postponed examination and induction until a course of training had been completed, or (c) because of employment in war industry or agriculture.

In September, 1942 the War Department announced that the Army would accept men with uncomplicated gonorrhea in a number not to exceed 2 per cent of the daily induction at each induction station for each race, the proportion to be determined by available hospital facilities. During February, 1943 the induction of registrants with uncomplicated syphilis began. Previously these diseases had been cause for rejection.

Among the white youths, craftsmen, foremen, and kindred workers (comprising skilled workers) had the lowest rejection rate, 19.9 rejections per 100 examined; farmers, with 36.4, and emergency workers, with 37.2 rejections per 100 examined, had the highest rates of rejection. Among the negroes, proprietors, clerks, salesmen, and kindred workers, with 26.9 rejections per 100 examined, and students, with 31.6 per 100 examined, had the lowest rejection rates; farmers, with 58.0 rejections per 100, had the highest rejection rates.

The ten leading causes of rejection among white eighteen- and nineteen-year-old Selective Service registrants were, in decreasing order of occurrence, as follows: eye defects, mental disease, musculoskeletal defects, cardiovascular defects, ear defects, hernia, neurological defects, educational deficiency, underweight, and mental deficiency. For eighteen- and nineteen-year-old negroes the ten leading causes of rejection were educational deficiency, syphilis, cardiovascular defects, mental disease, musculoskeletal defects, hernia, eye defects, neurological defects, mental deficiency, and tuberculosis. Half of the rejections of negro youths resulted from educational deficiency or from syphilis. These data are based on local-board and induction-station examinations made during December, 1942 and January and February of 1943.

White youths had higher rejection rates than negroes in defects of the following organs: eyes, ears, nose, kidneys, nervous system, feet, and endocrine glands; overweight and underweight were also found in greater proportion among white youths.

In the following broad groups of defects, negro youths had higher rejection rates than white youths: tuberculosis, cardiovascular disease, hernia, genital disease, syphilis, gonorrhea, skin disease, educational deficiency, mental deficiency, and mental disease. JOHN E. KIRKPATRICK, M.D.

Carmody, J. T. B.: War Wounds of the Head. *U. S. Naval M. Bull.*, 1943, 41: 1227.

This report deals with 12 cases of major gunshot wounds of the head admitted to a major base from the Guadalcanal campaign. No definite statistics concerning the incidence or mortality rate of gunshot wounds of the head are available, but it was the opinion of the medical officers who took active part that head wounds formed a small percentage of the total and that the fatalities resulted primarily from a direct hit by high-velocity fire.

Patients with head wounds were given first-aid treatment consisting of the local application of sulfanilamide powder followed by a compression head dressing. They were then moved through the various substations, where plasma was always administered, to the division hospital. Here the more seriously wounded were put in the best possible condition for plane transportation to the nearest base. Further care was given, and, when necessary, débridement of the wound was carried out. Those patients who could not return to active duty within a reasonable period were next transported to one of the major bases. An interval of from two to three weeks usually elapsed before casualties of this type arrived at a major base.

The seriousness of the condition of these patients and the severity of the cranial involvement were not due to the initial injury alone, but were primarily due to the development of complications. Osteomyelitis, retained fragments of bone and foreign bodies, brain abscess, and meningitis were the most common complications. All patients required operation, and some required several operative procedures. Two

patients with closed wounds which were free of infection had had compound comminuted depressed fractures of the skull and laceration of the brain. Operative repair in these cases was accomplished without incident. Of the 10 remaining patients, 7 were placed on the "serious list" on admission, and all had the common finding of osteomyelitis of the skull. Several of these cases are reported in detail. There were no deaths in the entire series.

During the First World War the mortality rate of major gunshot wounds of the head approached 60 per cent. There was a relationship between this excessive figure and infection, the time element before operation being an important factor. These cases are comparable to those of the last war in that they were major problems on admission as a result of infection. Chemotherapy and the alteration of the time factor by plane transportation of the wounded are the outstanding differences in treatment since World War I. Sulfa treatment has not eliminated infection but it may have been effective in hindering rapid progression of the infection. Since no definite statistics are available, it is assumed that the incidence of infection is definitely less than that existing before the general use of chemotherapy. The best results appear to have been obtained with sulfanilamide in powder form, given locally, and with sulfadiazine given by mouth. JOHN L. LINDQUIST, M.D.

Ascroft, P. B.: Treatment of Head Wounds due to Missiles: Analysis of 500 Cases. *Lancet*, 1943, 245: 211.

This article describes in detail the methods of treating missile wounds of the head as evolved from two years of experience in the battle area of the Middle East. The case histories of 516 patients wounded in battle are analyzed.

The principles of treatment are influenced as much by local conditions as by the nature of the wounds. In general, early excision of devitalized tissue prevents sepsis in wounds of the head no less than in those of other parts of the body. There are, however, certain peculiarities of structure and function of the brain and its covering which influence the behavior of head wounds and their treatment. First, the rich blood supply of the scalp, the intact dura, and the meninges are powerful barriers to the spread of infection. Secondly, the tissue of the brain resists infection well, but the products of trauma and inflammation should not be allowed to accumulate under pressure. Moreover, it must be remembered that continued exposure of the brain in an open wound is always harmful and is always associated with some degree of infection. Organic damage to the brain is irreparable, and even the gentlest surgical manipulation is damaging to some degree. Finally, it is considered that surgical manipulation within the skull cannot be carried out effectively without preliminary roentgenograms and special apparatus such as a mechanical sucker.

Head wounds which are not immediately fatal are less lethal and crippling than is popularly believed. The proportion of men who return to duty even after severe penetrating injuries, is much higher than was anticipated. Of the 516 patients, only 46 died and 44 of these had had the dura pierced.

FIRST-AID PROCEDURE

The procedure followed in handling these cases involves first aid, and when this is given the patient's general condition is appraised, and particular note is taken of the degree of shock, depth of coma, nature of the head wound, and other injuries that might be present. The hair is shaved around the wound and sulfanilamide powder is liberally applied, after which a field dressing is firmly secured to the head. Shock is seldom severe in head wounds, but when present it is usually due to loss of blood. Hence, whole blood is administered.

The patient is now evacuated to a base hospital area. It is believed that it is better not to operate in forward areas provided that the patient can reach a fully equipped base hospital within from forty-eight to seventy-two hours of the injury.

TREATMENT AT THE BASE HOSPITAL

Treatment at the base hospital consists in assessing the needs of the patient regarding resuscitation, level of consciousness, and priority in going to operation. All patients with head injuries are given complete x-ray study.

The urgency of operation depends largely upon whether the dura is penetrated or not, the degree of damage to the brain, and the number of indriven fragments of bone.

The nervous system is examined in detail. Frequently the path taken by the indriven fragments and metal can be predetermined by the neurological findings in this examination. The presence of unnoticed wounds or complications such as intracranial hemorrhage, the degree of consciousness, and the changes in the state of consciousness are recorded.

The inspection of the wound should be close enough to observe whether there is any cerebrospinal fluid leakage, a grave sign which indicates opening of the ventricular system.

Injuries of other parts of the body may be overlooked, especially when the patient is unconscious. Therefore, a general examination of the whole body is in order, with particular attention to the nose, eyes, and ears.

The value of lumbar puncture before primary operation is limited. There is one exception—if cerebral compression due to intracranial hemorrhage is suspected. This condition demands urgent operative relief.

OPERATIVE PROCEDURE

Preparation for operation includes the choice of anesthesia (excellent anesthesia is obtained by the use of sodium pentothal) and meticulous shaving, cleansing, and draping of the operative field.

A study of the roentgenograms and the passage of a probe through the wound will determine the site of

the fracture. The wound is narrowly excised, and careful search is made for hair, dirt, and debris that might have been driven in by the missile. Devitalized and cooked tissue is conservatively cut away. The damaged bone is removed only to the extent of the inner table.

THE TREATMENT OF SPECIAL TYPES OF FRACTURES

The treatment of the following special types of fractures is discussed: linear fractures; depressed fractures without loss of substance, such as (a) the rosette and gutter types, (b) the pond, or stove-in types, and (c) fracture of the inner table alone; fractures with penetration of bone into the brain substance; furrow fracture (from tangential missiles); elevated fractures, including the bursting and slicing types; and fractures with a foreign body retained in the bone.

The surgical management of the lesion is influenced by the condition of the dura (whether it is intact, or obviously or only inconspicuously torn) and of the brain. If the missile track is deep, with through-and-through penetration, it may not be possible to cleanse the track effectively. Effective cleansing of large cavities may also be impossible. Extensive superficial wounds, on the other hand, though formidable at times, are less often fatal or even crippling, and isolated fragments of metal seldom cause trouble, and are best let alone.

Hemostasis is most important and is difficult to obtain without electrocoagulation. Large vessels are secured with Cushing's silver clips. Closure of the wound includes adequate drainage. Plastic repair of the bone has no place in this type of surgery. Approximation of the muscles and scalp without tension is extremely important.

POSTOPERATIVE TREATMENT

Nursing the stuporous patient through to consciousness demands the utmost effort on the part of the nursing staff. Administration of fluids and food requires skill and training. The choice of sedative is most important, and requires mature judgment.

The policy of returning men early to activity is founded upon the belief that the minimizing of the significance of the injury to the brain produces more good than harm.

Convalescent patients are encouraged to assume useful odd jobs about the hospital, which afford physical exercise and help to bolster morale.

STEPHEN A. ZIEMAN, M.D.

Peiper, H.: How Should a Recent Brain Injury Be Treated? (Wie soll der frische Hirnschuss operiert werden?) *Deut. med. Wschr.*, 1942, 68: 1233.

Experience showed that a primary suture in brain injuries may be employed not only within the twelve-hour period but within the first forty-eight hours in selected cases, provided that a drain is placed under the skin. If the general condition does not prohibit operation, it is indicated in all head injuries because even after injuries by a revolver bullet an abscess or a small prolapse of the brain may form. The purpose of an operation is chiefly the avoidance of a secondary infection. Small wounds are excised under local anesthesia and the bone is explored; if an injury of the bone is found, two perpendicular incisions are made to form an H-shaped wound. If a more extensive injury is present, the excised wound is closed immediately following the formation of a flap consisting of skin and galea, and before exploration of the brain. The defect in the skull is enlarged with Luer's forceps and depressed bone fragments are carefully removed. Epidural hematomas are removed and small tears of the dura are sutured. As a rule, the author does not incise the dura which is apparently intact, in order to avoid formation of a scar or a cyst; this is contrary to the practice of Vincent who advocates an excision of the area of cerebral contusion. The dura is sutured with silk; if the defect is large, a plastic operation employing the galea is indicated. A restitution of the injured dura is considered by the author as one of the most important operative procedures because the dura prevents a prolapse of the brain, protects the brain against infection, and avoids the formation of a fistula if one of the ventricles is injured. Moreover, the dura prevents the formation of a scar between the skin and the brain.

Suction is employed to cleanse brain wounds; in search for bone fragments, palpation with the finger is preferable to the use of instruments. Hemorrhage is stopped by the application of cotton pledgets soaked in hot saline solution; or small particles of muscles, diathermy, or silver clips may be employed in some instances.

Sulfonamides are applied at the end of the operation.

In the presence of recent prolapse of the brain, the bone is excised around it and the defect in the skull is enlarged until an intact dura is exposed. The prolapse is removed at the skin level and suction is applied to the adjoining area of the brain. The defect is covered by using a flap formed by skin and galea.

All injuries of the base of the skull require an immediate operation because of the danger resulting from an injury of the frontal, sphenoid, or ethmoid sinuses. Co-operation with otologists and ophthalmologists is essential.

Traumatic edema of the brain and intensified production of the cerebrospinal fluid usually continues from two to three weeks and may be combated by repeated suboccipital puncture. This procedure is also a good prophylactic measure against meningitis. As a rule, from 15 to 30 cc. of fluid are withdrawn every second day until the increased pressure subsides, the xanthochromatic color of the fluid disappears, and the general condition of the patient improves. The postoperative treatment comprises also the prophylactic use of sulfonamides, the employment of strophantine, and the intravenous injection of 10 per cent calcium or from 40 to 50 per cent glucose solution. JOSEPH K. NARAT, M.D.

Theis, F. V.: Atmospheric and Immersion Blast Injuries. *War Med.*, Chic., 1943, 4: 262.

Atmospheric and immersion high explosive blasts produce injuries to the internal structures of the exposed body with absence of external trauma. The various factors contributing to the extent, severity, and distribution of the pathological lesions are discussed.

There is no essential difference between the injuries resulting from atmospheric blasts and those due to immersion blasts. The physics of explosive blasts and the mechanism of injury to the body are described.

The symptoms will indicate the extent and severity of the pathological lesions. Knowledge of the type of lesions produced by blast waves will be helpful in interpreting the symptoms and in making a diagnosis.

Treatment includes both prophylactic and active measures to reduce the frequency and the seriousness of blast injuries. It is summarized as follows:

In order to avoid or decrease the serious effect of blast on the body some protective measures can be taken. In the presence of an impending blast it is advisable to exhale forcibly and contract the abdominal muscles.

For atmospheric blasts protection is afforded by shelters, heavy clothing, and cotton or plastic appliances for the ears. By lying face down in a gutter or trench one protects the less shielded parts of the body, such as the abdomen and chest, which may be more seriously injured. In the presence of immersion blasts, one should keep the head and as much of the body as possible out of water by swimming on one's back and should keep the mouth open. It is advisable to wear a heavy kapok life jacket and delay getting into the water as long as possible when immersion blasts are expected.

Appropriate treatment depends on the extent, severity, and distribution of the injuries.

For shock immediate treatment consists of administering morphine in adequate doses; supplying plasma, whole blood, water, or physiological solution of sodium chloride in adequate amounts; applying external heat; placing the patient in the Trendelenburg position, and administering oxygen when this is necessary.

For injury to the lungs treatment is expectant and conservative, with absolute rest and quiet. In addition, inhalation of oxygen will relieve respiratory difficulty, especially when severe pulmonary damage has occurred. Lockwood advised direct inflation of the lungs, especially in cases of pulmonary collapse, by blowing into the patient's mouth. This measure is of questionable value, and when extensive alveolar rupture has occurred it is dangerous because of the possibility of air embolism.

Fluids and food should not be given by mouth until the extent of intestinal injury is determined. Wangensteen continuous gastric and intestinal aspiration has proved of value in relieving distention incident to paralytic ileus and the resulting danger of intestinal perforation. The reduction in intraluminal pressure will relieve the tension on devitalized areas of traumatized intestines.

Perforation of the tympanic membrane usually heals without permanent disability unless infection supervenes. Instillations of any kind definitely contribute to infection of the traumatized ear and therefore are condemned. Small wicks of sterile cotton in petrolatum lightly placed in the external canal and frequently changed have proved safe and satisfactory.

Although exploratory operation for suspected intestinal perforation may be necessary, it should be kept in mind that few patients have been benefited by operation. Despite the urgency and seriousn ss of the abdominal symptoms, most of the patients have recovered without operation. However, intestinal perforations and localized intraperitoneal abscesses require surgical treatment. Inhalation anesthesia should be avoided because of associated pulmonary lesions. J. M. MORA, M.D.

Bywaters, E. G. L., Crooke, A. C., and Morris, C. J. O. R.: Limb Compression in the Tube-Shelter Disaster. Note on Plasma Volume Determinations. *Lancet*, 1943, 245: 373.

Among 60 injured survivors of a shelter disaster in which more than 200 people were tightly packed from one and a half to two hours, 12 were seen by the authors.

One patient died of other injuries soon after release, but presented remarkable ischemic necroses of the muscles, which were clearly pressure necroses and identical with those seen in persons pinned down by beams and debris in air raids. These necroses were regarded as the basis for myohemoglobinuria and the subsequent suppression of urine. From this case it was concluded that muscle degeneration may follow compression for two hours without a violent "crush" such as occurs when large blocks of masonry fall. One patient developed a high grade of uremia but ultimately recovered; 10 others who recovered showed every grade of injury from severe muscle damage to skin erythema only. Even the brief period of compression caused a demonstrable evidence of plasma loss, although there was no fall in the blood pressure to shock levels.

Most cases of crush syndrome proper occur in patients who have been severely injured, with gross, and often progressive, limb swelling, with clinical shock, manifested by a thready pulse and decreased blood pressure, and with renal function which has been impaired sufficiently to produce a high degree of uremia or death. Minor grades of damage are being recognized more frequently but they often pass unrecognized until uremia or death occurs. The diagnosis can now be made earlier with detailed biochemical determinations and detection of pigment excretion following injury.

Observations of the degree of hemoconcentration, blood-urea rise, and creatine excretion indicate that while little damage is done by compressions of an

hour or less, maximal damage is produced by compression for three hours or more; the critical period, in which ischemia produces irreversible changes, seems to be in between these two time limits. The exact length of the critical period may be determined by such factors as temperature.

The period of compression in this series was brief. It lasted for a shorter time than that of any of the previously observed cases of limb compression due to falling masonry, and may have been related to the mild degree of damage and absence of shock. It seems possible that for periods shorter than from two to three hours, the ischemia might be insufficient to produce local necrosis with the accumulation of much local fluid, but adequate to produce a local increase of cell permeability with loss of pigment.

The chief variable other than the duration of the compression affecting the severity of the lesion is, from clinical experience, the amount of muscle damaged. A good index to this is the amount of myohemoglobin and creatine that is released. The authors have noticed, however, that with renal impairment only a small portion of the pigment is excreted. They claim to have shown that the renal damage in animals with acid urine is not related to the amount of pigment injected, nor to the amount of pigment excreted, but to the amount retained. It is difficult to decide whether the pigment initiates renal failure, or whether the pigment is retained because of renal failure.

Five patients, whose urine was rapidly made alkaline, showed no renal failure, whereas 1 patient who had been subjected to exactly the same trauma of similar duration and extent, but without alkalinization, subsequently developed uremia.

It was the authors' belief that quantitative estimation of myohemoglobin, creatine, and potassium excretion gave a basis for the calculation of the amount of muscle damaged, and that this was the best guide to the severity of the lesion. These excretions ran parallel to the duration of albuminuria, and to the local plasma loss.

LeRoy J. Kleinsasser, M.D.

Traube, V.: The Surgical Treatment of Infected Bullet Wounds of the Knee (Chirurgische Behandlung von infizierten Kniegelenksschuessen). *Deut. med. Wschr.*, 1942, 68: 982.

Surgical treatment of recent injuries of the knee articulation should be conservative provided that there is no fragmentation of the articular surfaces and no foreign body is lodged within the articular space. The entire extremity should be immobilized in a slightly flexed position, in a body cast, and the exudate aspirated two or three times. For prophylactic purposes 1 or 2 cc. of Chlumsky's solution should be injected at the time of aspiration.

If an injury in a tangential direction caused an extensive tear of the articular capsule, it should be sutured. If the defect cannot be corrected in this manner, a plastic operation should be performed by utilizing a flap consisting of skin and fat. After the operation 1 or 2 cc. of Chlumsky's solution should be injected into the articulation and a body cast applied to the injured extremity.

If a missile is lodged in the articulation or if fragments of articular surfaces are loose, the joint is exposed through an S-shaped incision and the foreign bodies are removed; the articular capsule is sutured and the wound closed in layers after the injection of Chlumsky's solution; a body cast is then applied.

If an empyema forms but is confined to the upper recessus and the anterior pocket, Payr's drainage is instituted by introducing a glass or rubber tube into the articulation through a stab incision. After aspiration of the purulent exudate, the articulation is irrigated with a 0.5 per cent procaine solution and filled with the same solution to which 2 cc. of Chlumsky's solution has been added. The drain is closed with a cork and the whole extremity is splinted. The articulation is refilled with the aforementioned solution daily for five or six days and thereafter every two or three days until a cure is obtained.

If a neglected empyema spreads to the lower posterior recessus, the intra-articular ligamentary apparatus becomes involved and the threatened capsular phlegmon with para-articular abscesses is the result. Usually a spontaneous perforation through the posterior pockets of the capsule takes place. The pus may also reach the anterior popliteal bursa, with a resulting infection of the interspaces between the flexor muscles of the calf. From the upper recessus the pus finds its way to the linea aspera and into the posterior and outer aspects of the thigh, forming a so-called tubular abscess. If a capsular phlegmon or panarthritis develops, either a horizontal resection of the condyles or a partial resection of the knee comes into consideration. The first mentioned operation is employed by the author if the fragmentation of the articular spaces and damage to soft tissue is not considerable and the intra-articular ligamentary apparatus is intact. This operation offers the following advantages: (1) the lowest part of the articulation is treated, (2) the intra-articular and extra-articular ligamentary apparatuses remain intact, and (3) no shortening of the extremity results. With the knee in a slightly flexed position each condyle is resected through separate horizontal incisions; the lower portion of the menisci is also removed and in addition a posterior arthrotomy is performed. Rubber drains are introduced into the empty spaces created by removal of the condyles, and the extremity is immobilized in a body cast. The postoperative treatment consists of irrigation of the articulation through the rubber drains with rivanol solution.

More extensive injuries require a partial resection of the articulation. The disadvantages of this method are: (1) possible subluxation of the tibia, and (2) shortening of the involved extremity. After the operation the joint is irrigated twice a week with rivanol solution. If the pain does not subside and the septic appearance of the patient does not improve

three or four days after the operation, an amputation of the thigh is indicated. On the other hand, a high temperature alone is not alarming because it usually lasts two or three weeks. JOSEPH K. NARAT, M.D.

Wustmann, O.: The Treatment of Phlegmones and Abscesses after Infected Bullet Wounds of the Lower Extremities (Die Behandlung von Phlegmonen und Abszessen nach infizierten Schussbruechen der unteren Gliedmassen). *Deut. med. Wschr.*, 1942, 68: 1050.

All injuries of the thighs may be divided into (1) those caused by large missiles, (2) those without suppuration, and (3) infected bullet wounds. In the author's material 75 per cent of the wounds were infected and, on the whole, the sulfonamide treatment of infected wounds was disappointing.

Not only from the anatomic but also from the clinical point of view, bullet wounds of the thigh may be divided into those of the upper, middle, and lower thirds. The first group is least dangerous, possibly because of the relatively superficial location of the bone in this region, with the resulting accessibility and the ease of removal of the hematoma. The quicker the hematoma is removed through a lateral incision, 15 cm. long, the prompter the cure; otherwise an abscess complicates the condition. As a rule, an infection of a fracture of the femur leads to the formation of an abscess which spreads in one of the three following directions: (1) along the quadratus and abductor minimus muscles to the subgluteal space; (2) along the vastus intermedius and fibularis muscles or (3) along the insertion of the ileopsoas muscle.

As a rule, an infected bullet wound of the femur requires twice as much time for healing as a common fracture encountered in industrial surgery.

In the middle and lower thirds the bone is embedded in deep muscle masses which may be damaged badly and cause severe hemorrhages; furthermore, large vessels located close to the bone may be injured by the missile or bone fragments. Hematomas may attain large sizes, produce ischemia, and facilitate infection. The author aspirated such hematomas one or two days after the injury and found all of them infected. He recommends a lateral incision and removal of the hematoma in each fracture of the femur in which an infection is suspected. Tubular abscesses require counter-incision, which should never be placed in the region of the femoral triangle on the median or anterior aspect of the thigh because hemorrhage may be caused by erosion.

A fracture in the lower third of the femur usually causes a posterior displacement of the distal fragment, and if a cast is applied with the knee extended, the femoral artery may be injured by the sharp edge of the lower fragment. An abscess forming from a hematoma after a supracondylar fracture usually spreads toward the vastus lateralis muscle; occasionally the abscess spreads in the distal direction along the vastus medialis and lateralis muscles toward the knee, and perforates the popliteal space. Median and lateral incisions should be used to open such abscesses.

All infected fractures of the femur are treated without dressings.

Of 310 patients with injuries of the upper leg, 13, or 4.10 per cent, died, while of 248 patients with fractures of the lower leg only 1, or 0.4 per cent, died.

Incisions in the treatment of infected fractures of the lower legs are employed by the author only exceptionally since the introduction of Dakin's irrigation method. JOSEPH K. NARAT, M.D.

Sylla, A.: Causes, Prophylaxis, and Treatment of Gangrene of the Extremities in Exanthematic Typhus (Ursachen, Verhuetung und Behandlung der Gliedmassengangraen beim Fleckfieber). *Deut. med. Wschr.*, 1942, 68: 1185.

Exanthematic fever has a tendency to produce gangrene, especially of the lower extremities. The gangrene may affect only the skin or also the deeper layers, involving the toes or the entire foot and a part of the lower leg. The author observed also a bilateral gangrene.

Relatively frequently patients suffering from typhus complain of pains in the lower extremities. The feet are cold and the pulse of the dorsal artery of the foot is very weak. Probably the pains are of an ischemic character. As a rule, gangrene appears from eleven to thirteen days after the onset of the disease, and is accompanied by a rise in the temperature. The indications for operation are the same as in diabetic gangrene. Usually thrombi are found only in small arteries, and it follows that a thrombosis or an embolism of an artery cannot be considered as the cause of gangrene. Examination of the eyegrounds shows a narrowing of the artery in 10 per cent of the cases, apparently due to a spasm of the afferent vessels. Probably a toxic effect of the typhus on the central nervous system causes a vasomotor disturbance, which however cannot be considered as the sole cause of the gangrene.

Gangrene was observed by the author almost exclusively during the winter months. Probably a combination of the toxic effect of the typhus, irritation of the midbrain and medulla oblongata by typhus nodules, and exposure to cold cause the gangrene.

Typhus patients should be kept in warm rooms. Attention must be paid to their feet, which should be well covered. If the extremities become cold and the pulse of the dorsal artery becomes weak, a heat cradle should be applied or the extremity should be packed in cotton. Pains caused by a spastic condition of the vessels may be relieved by injections of a pancreatic extract called padutin. Progynon or testicular hormone, or a combination of both of them may also be helpful in the early stages of the condition. If gangrene develops, 75 cc. of a 0.25 per cent procaine solution without adrenaline should be injected in the paravertebral spaces and 200 cc. should be injected around the involved extremity

above the gangrene. If the circulation improves, the injection should be repeated on the two following days. JOSEPH K. NARAT, M.D.

Hill, L. W., and Lever, H. S.: Meningococcic Infection in an Army Camp. *J. Am. M. Ass.*, 1943, 123: 9.

The authors believe that infection with the meningococcus is divided into three stages: (1) nasopharyngeal infection, differing in no way, clinically, from such conditions produced by other organisms; (2) the stage of septicemia; and (3) the stage of meningitis.

The onset of meningococcic infection was gradual in about half of the cases studied, sudden in the rest. The severity of the subsequent disease could not be correlated with its early manifestations. The cardinal symptoms and signs were headache, vomiting, chills, and rash. Accessory symptoms were conjunctivitis, nasopharyngitis, sore throat, drowsiness with inability to concentrate, backache, myalgia, arthralgia, stupor, delirium, or coma. Most patients had a characteristic pallor and looked ill and toxic despite low temperatures and pulse rates.

Headache was present in all cases and varied from moderate to excruciating in severity. Vomiting was the second most important cardinal symptom. The rash was present in all but 9 cases, and ranged from profuse petechiae and purpura to faint pink macules.

The blood leucocyte count ranged from 7,000 to 48,000 and in 30 cases was over 20,000. The blood culture was positive in 40 of 68 cases. The blood-sugar level was normal or increased in the cases in which this study was performed. The spinal fluid was clear in 31 of 62 cases in which it was examined. When the leucocyte count exceeded 500 the spinal fluid was opalescent; it was noticeably cloudy if the count was over 1,000. The percentage of polymorphonuclear cells in the spinal fluid varied from 20 to 100. Smears of the spinal fluid were positive for the meningococcus in only 38 of 62 cases; cultures were positive in 29 cases. Quantitative determination of the spinal-fluid sugar revealed a decrease from the normal in 22 of 47 cases. The globulin was increased in 24 of 47 instances.

The method of treatment is outlined in some detail. The initial dose of sulfadiazine was 5 gm. in 100 cc. of distilled water, given intravenously, followed by 1,000 cc. of 5 per cent dextrose in an isotonic solution of sodium chloride. Eight hours later 2.5 gm. of sodium sulfadiazine were given in a similar manner, and the same dose was repeated eight hours later. If at the end of another eight hours the patient was unable to tolerate this medication by mouth, the same dose was repeated. If the patient's condition was satisfactory eight hours after the third dose, oral administration of the drug was started, and 1.5 gm. were given every four hours. Two days after the temperature receded, the interval was changed to every six hours.

The authors do not like to see the blood concentration of sulfadiazine fall below 8 mgm. per 100 cc. If the patient exhibited evidence of circulatory failure, 1,500 cc. of 5 per cent dextrose in an isotonic solution of sodium chloride was given intravenously, and 2 cc. of adrenal-cortex extract were given hypodermically as often as was required. The duration of drug treatment averaged eleven days; the total amount of drug, from 60 to 70 gm.

HAROLD C. OCHSNER, M.D.

Daniels, W. B., Solomon, S., and Jaquette, W. A., Jr.: Meningococcal Infection in Soldiers. *J. Am. M. Ass.*, 1943, 123: 1.

One hundred and twelve patients with meningococcal infection were studied at the Station Hospital at Fort Bragg. Eighty had meningitis and 32 had bacteriemia without localization in the meninges. The soldiers who were in the service less than three years furnished 59 per cent of all the patients with meningococcal infection.

The course of events consists of an invasion of the blood stream and, if not prevented by spontaneous resistance or therapy, localization in the meninges, joints, skin, eyes, or other body tissues occurs. It is highly important that the stage of sepsis be recognized early and that the patient be treated promptly. In this way the disease can usually be terminated before localization in the meninges occurs. In this series, 35 per cent of the cases were recognized in the stage of sepsis.

Diagnosis of meningococcemia without meningitis was made in 32 cases. In 78 per cent of these patients, respiratory symptoms were present—on the average, six days prior to the diagnosis. Feverishness was noted for an average of three days. The incidence of headache was high. Nausea occurred in 59 per cent of the patients. The most characteristic manifestation was the rash which at times, however, was so sparse that careful search was necessary to find it, yet at other times it was very obvious. The most common lesion was petechial or purpuric and varied from 1 to 15 mm. in diameter. Ill-defined faint pink macules similar to the rose spots of typhoid were common. The larger ones of this type were nodular or plaquelike, and often tender; when they were on the extremities they resembled the smaller lesions of erythema nodosum. Herpes simplex was common, usually occurring about the second day of the illness. The admission temperature was generally between 101° and 102° F. The average leucocyte count was 17,000 per c.mm. The blood culture was positive for meningococci in 56 per cent of the cases. In every case the spinal fluid was normal.

The prodromal symptoms of the patients who developed meningitis were similar to those of the patients with uncomplicated meningococcemia. The average duration of the respiratory complaints was eleven days. Fever was present for three days prior to the diagnosis. In 36 per cent of the patients a shaking chill preceded the onset of the meningitis. The initial leucocyte count averaged 21,600 per c.mm. The average spinal-fluid leucocyte count was

6,800. There was no constant relation between the level of sugar in the spinal fluid and the severity of the disease. Meningococci were demonstrated on smear of the spinal fluid in 77 per cent of the cases, and on culture in 81 per cent. Blood culture was positive in 40 per cent. The meningococcus was not grown from the blood or spinal fluid of any patient who had been treated with a sulfonamide compound prior to culture.

Cases illustrative of variations in meningococcemia, of transition from sepsis to meningitis, and of the most common type of meningitis are reported.

In the cases of uncomplicated meningococcemia an initial dose of 4 gm. of sulfadiazine was given, followed by 1 gm. every four hours until the temperature had been normal for two days. Parenteral administration was resorted to when patients were vomiting.

Of the 80 patients with meningitis, 78 were treated with sulfadiazine; the other 2 received sulfapyridine and recovered. The first 45 of those treated with sulfadiazine were given approximately twice as much of the drug as the last 33. In the former group, an attempt was made to maintain the blood concentration at 15 mgm. per 100 cc., and in the latter group at 8 mgm. The patients treated with the lower dose of sulfadiazine responded as well or better than the group treated with higher doses. To attain the lower blood concentration of sulfadiazine the patients received an initial "loading" dose of 0.05 gm. of sodium sulfadiazine per kgm. of body weight intravenously, and four hours later a dose of 0.025 gm. per kgm. of body weight subcutaneously. This dose was then repeated every eight hours until the patient could retain the drug given by mouth. One gram of sulfadiazine was then given every four hours until the temperature had been normal from five to seven days. The fluid intake was maintained at 4,000 cc. daily and the urine output at 1,200 cc. or more. In the 80 cases of meningococcic meningitis the mortality rate was 1.25 per cent. HAROLD C. OCHSNER, M.D.

Debenham, R. K.: War Surgery in the Middle East. *British M. J.*, 1943, 2: 223.

As a result of three battles—Tobruk, and the first and second El Alamein—3,479 casualties were received in a Middle East front-line hospital. All types of injuries were seen under various and changing conditions.

The system of handling these cases proved most efficient, and was carried out by a sorting officer who appraised the case and allocated it to the proper service for disposition according to priority, an operating team, and an orderly who saw that the operating team was not delayed by waiting for the arrival of patients.

The following wounds were treated:

Flesh wounds. Minor flesh wounds constituted by far the largest number of injuries. Treatment consisted primarily in minimizing the possibility of infection, conservative excision, and the establishment of adequate drainage when this was indicated. There was no prolonged search for foreign bodies. It was found that in war wounds, no sutures should be used, nor should packing be employed unless it is necessary for the control of hemorrhage.

Fractures. The use of a sound part of the body for splinting purposes was frequent in forward areas. The usual splints, plaster casts, and bandages were freely applied.

Head wounds. A common injury was a small penetrating wound of the head just under the side of the helmet. A fragment of the shell may have lodged in the brain. Treatment was essentially an attempt to get the wound to heal by first intention and so prevent escape of cerebrospinal fluid and the onset of meningitis. Sulfanilamide was dusted in the wound and the scalp was closed in two layers.

Neck wounds. It was remarkable how important structures in the neck apparently escaped injury, but chest wounds constituted the greater proportion of the total number. Treatment of these wounds was almost entirely medical, and was carried out by the medical specialist.

Abdominal cases. Of the 300 cases received from Tobruk, 3 were injuries perforating the bowel, with 1 death. Of 2,287 casualties from the first battle of El Alamein, 8 received perforating wounds with 3 deaths. Among the 500 casualties from the second battle of El Alamein there were 30 perforating thoracoabdominal or abdominal wounds.

Wounds of the buttocks, genitourinary organs, and spine. The chief point to remember about buttock wounds is that the missile may have penetrated into the pelvis and injured the bowel or bladder. A wound of the genital organs is likely to involve also the cave of Retzius, the urethra, and perhaps the bladder. Wounds of the spine are usually associated with complete paraplegia, and are apt to arrive during rush periods when there is little time to deal with them. In the few cases in which operation was performed it was usually found that pressure on the spinal cord was produced by bone fragments and not by the missile itself. Suprapubic cystotomy is often necessary in these cases.

Vascular lesions; amputation. Ligature of a main vessel with extensive damage to the limb distal to it is fraught with grave danger and usually ends with amputation. The chief points concerning amputation are as follows: the limb should not be removed at the site of election, for infection is almost sure to follow; the maximum length of limb should be preserved, because secondary amputation is often necessary; some form of flap should be fashioned, as guillotine amputation is very painful—the flaps should not be sutured; and the best dressing is probably a vaselined gauze pack.

Nerve lesions. Lesions of the ulnar and musculospiral nerves were common; the median nerve was less often involved. Musculospiral lesions were not always due to the wound itself, but sometimes due to pressure, e.g., if the limb was allowed to hang over the operating table. External popliteal lesions were

frequent also, and occasionally the whole sciatic nerve was paralyzed.

Burns. The worst cases of burns came from fighting in tanks. Almost all the burns seen during the period under review had been cleaned up more or less, then powdered with sulfanilamide and dressed with vaselined gauze. Patients travelled best with plenty of padding, and in the case of the limbs, a light, well padded plaster-of-Paris cast was definitely beneficial. In the early stages plenty of intravenous plasma or serum was essential.

General treatment included good nursing care. In all, 328 pints of blood (mostly stored) and 96 pints of plasma or serum were used, apart from a considerable quantity of 5 per cent glucose in N/5 saline solution. Transfusions were used for shock, for burns, and during convalescence when the hemoglobin fell below 60 per cent. Gas gangrene in the true sense was very rare, and gas infection uncommon. No case of tetanus was seen. Pentothal was the anesthetic of choice, especially for short operations. Only a very light anesthesia was required for most cases, and the tired wounded man was easily and quickly anesthetized. There were 97 deaths in all, a mortality of 3 per cent in the battle of Tobruk, of 1.3 per cent in the first battle of El Alamein, and of 10 per cent in the second battle of El Alamein.

The following "Don'ts" conclude the essay:

Don't suture wounds.

Don't suture amputation stumps.

Don't amputate at the site of election; go below it.

Don't use packing except to stop hemorrhage.

Don't use drainage tubing.

Don't use unpadded plasters.

Don't let a plaster dry with the heel resting on the stretcher.

Don't forget to give morphine before a long, bumpy journey.

Don't forget to sling a Thomas splint on the stretcher bar.

Don't forget to give plenty of fluids by mouth.

Don't forget that the ligature of a main vessel should be prominently recorded on the field medical card and underlined. Gangrene is very dangerous.

STEPHEN A. ZIEMAN, M.D.

British Surgeons' Visit to U. S. S. R.: Impressions of Soviet Medical Organization. *Brit. M. J.*, 1943, 2: 208.

The four British surgeons who have been paying a three-weeks' visit to Soviet Russia attended a reception given in their honor by the British Council immediately upon their return, and gave the assembled company some account of their experiences This British mission was sponsored jointly by the British Council and the Medical Research Council, and its members were Surg. Rear-Adml. G. Gordon-Taylor, consulting surgeon to the Royal Navy; Mr. E. Rock Carling, consultant adviser to the Ministry of Health, the Ministry of Home Security, and the Ministry of Pensions; Major-Gen. D. C. Monro, consulting surgeon to the British Army (War Office); and Mr. R. W. Watson-Jones, civilian consultant in orthopedic surgery to the Royal Air Force. Two American surgeons, Lieut.-Col. Elliott and Lieut.-Col. Loyal Davis, and a Canadian surgeon, Prof. Wilder Penfield, accompanied them.

The visitors during their short stay in Russia inspected hospital arrangements as far forward as Vyazma on the Western front, visited the clearing, field, and mobile hospitals, and inspected the medical institutes and depots in Moscow. They found the organization of Russian medical services excellent. In their surgical work the Soviet medical service, with some differences in detail, follows the same general principles as those accepted in British war surgery, and has reached the same conclusions. The Commissar in charge of the service stated that at the time of the last war the Russians realized that their arrangements were not as good as those of their allies, and during the twenty-five years between the two wars they have set themselves to reach a standard of medical and surgical work which will bear comparison with that of any other belligerent country.

TWO IMPRESSIVE ORGANIZATIONS

Two points impressed the mission very greatly. One was the system of blood transfusion, which is carried out on a colossal scale. The arrangements for the collection of blood are beyond criticism, and the number of voluntary donors is very large. In one institution in Moscow a daily average of from 500 to 800 donors are bled, and 90 per cent of them are women. No woman is allowed to be bled more than seven times a year, but in practice, so large is the number of volunteers, they are not bled more than five times. They receive extra rations and also payment, but four-fifths of the money received is returned for war purposes. The same procedure is followed as in this country in the use of plasma and serum. In no circumstances has the Russian Army lacked transfusion blood. The blood is transported to the front by large airplanes and then to outlying parts by small airplanes. At one place on the front blood has actually been flown to small collections of wounded behind the German lines. The second point was the organization for getting special cases into the hands of specialists at the earliest possible moment and in the condition in which they liked to receive them. Even as near to the front as eight or ten kilometers the different kinds of cases according to the nature and location of the injury are segregated and placed in the hands of junior specialists, who, after early treatment, pass them on to their seniors at the special hospitals. There appears to have been no shortage of dressings or anesthetics. The Russians rely almost entirely on local and spinal anesthesia.

TRAINING OF PERSONNEL

As for the medical personnel, the chief of the medical services of the Russian Army, General Smirnov, is 35 years of age, and an expert opinion on

him given by an academician was that he not only was an admirable administrator but was held in the highest regard by his colleagues from the professional point of view. The medical service is becoming a woman's service; 90 per cent of the doctors now under training are women, as compared with 50 per cent in peacetime. The mission noted that some of the young women doctors carried as many as five wound stripes, which meant, not that they had received five wounds, but that they had been wounded five times. For doctors in Russia the ordinary course before the first State qualification is five years, comparable with our own requirement. It takes three years to get a bachelorship and three more years to get a doctor's degree. Nurses had three years' training before the war, and this is now reduced to two years.

The Russian nurse evoked the great admiration of the visitors. Not only is she excellent at the job for which she has been trained, but she can turn her hands in spare time to any employment, even to building hospitals, involving cutting down trees, squaring timber, making window and door frames, digging out foundations. She is specially expert in the art of camouflage. One of the members of the mission described how their car stopped at a place in the forest where, apparently, no building was in sight. Slowly it dawned upon them that they stood at the entrance to a 1,000-bed hospital so camouflaged as to appear part of the forest itself. Some of the trees had even been left standing inside the building, their tops growing out of the roof.

The visitors made as extensive an inspection as was possible during their brief stay, and only shortness of time prevented them from going to the Far East, where the convalescent cases are sent. They saw something of the research institutes and medical organization in Moscow, where the civil defence and ambulance arrangements impressed them. Five telephone operators are detailed every night to deal with emergency medical or surgical calls from any part of the city, and within two minutes of the receipt of the call a well-equipped ambulance, with doctor, nurse, and orderly, is on its way. In the control room there is an immense map of Moscow; on receipt of a call a button is pressed for the name of the street, and the street then appears illuminated on the map, and the nearest ambulance station and the quickest route are at once indicated.

It is hoped that a return visit of Soviet surgeons to this country will be arranged.

(ORIGINAL ARTICLE)

Watson-Jones, R.: Russian Surgeons and Russian Surgery. *Brit. M. J.*, 1943, 2: 276.

Mr. Watson-Jones was one of a group of British surgeons who recently visited the U.S.S.R. under the auspices of the Medical Research Council and the British Council, and has contributed the following article at our request.—Ed., *B.M.J.*

It is not easy to form an immediate impression of the people of Moscow because the closing of all shops except the few which supply food, the lack of color, lighting, decorating, and flowers, the striking disappearance of dogs, cats, and pets, so that I saw but one dog in three weeks, the wearing of shoddy clothes and footwear so that the Army might be well clad, and the limitation of amusement to an occasional seat at the ballet are the restrictions of war, and they emphasize unduly the solid, determined, plodding, almost expressionless features of men and women in the streets. Life in Russia has been hard; pleasures have been few. It is true that there is no sign of malnutrition; the rations of the worker are comparable with those in England; I searched for evidence of rickets and found none; the children are bright-eyed, healthy, and happy. But there have been privations, and the faces of the people show it; it is not always easy to know what they are thinking. Nevertheless one impression was quickly formed by the surgeons who represented England, Canada, and the United States in a recent visit to the Soviet Union. It was impossible to mistake the spirit of overwhelming hospitality with which we were received. It was impossible to misjudge the very cordial friendship which developed. From high officials of the Commissariat who received us at the airfield, to hotel staff members who apologized because they could offer no more than one hot bath a week; from generals who thought of our comfort during arduous journeys over shelled roads and demolished bridges, to soldiers from Stalingrad who insisted on our climbing and entering the mightiest tanks; from hospital superintendents and commanding officers whose invitation to a cup of tea implied a heavily laden table and a two-hour banquet, to attendants in the Park of Rest and Culture who were satisfied only when we shared the terrors of a dummy aircraft which simultaneously rolled and looped; from crowds at the Exhibition of Captured War Material whose smiling comments included the words "Angleeskee" and "Americanskee," to the handful of determined survivors remaining from the half-million inhabitants of demolished Vyasma; from all people and all professions we received the greatest kindness and the most convincing evidence of friendship and good will.

We formed a second, very vivid impression on seeing the astonishing capacity of Russian women for hard work. Men employed in repairing roads and relaying tram tracks worked with an intensity which reminded us of home; but the women who shared their strenuous task paused less often and were more consistent. Girls of 18 and 19 drive the trams and scramble on to the roofs to repair the trolley arm. Traffic is controlled by sturdy women police armed with a black-and-white striped truncheon and a pistol at the hip. Hundreds of miles of military roads are guarded by women soldiers with tommy guns. Women doctors, women surgeons, and nurses work in the front line; many of them wear the chevrons of multiple wounds. The Inspector-General of Medical Services of the Red Army is a woman.

FRONT-LINE HOSPITALS

Not only do nurses attend the wounded, but in the intervals of battle they build the hospitals. One of the front-line hospitals we visited is built in territory which until last March was occupied by the enemy; within four months a 2,000-bed hospital has been almost completed by nurses who are obviously skilled in the use of the saw, the plane, and the spirit level. Many of these hospitals are buried six feet deep and covered with a thin layer of soil and turf. They are constructed wholly of wood from the forests in which they are perfectly camouflaged. Trees standing within an inch or two of the walls are left undisturbed, and wards may even be built round living trees which grow out of the roof, only branches within the building being stripped.

The reception-sorting ward is completely free of all fixtures and equipped only with collapsible trestles on which stretchers are laid. Washing and shaving is recognized as an important first-aid measure, and part of the ward is devoted to baths, or rather there are places near the wall where hot water is sprayed over the wounded man as he lies on the stretcher. After the patient has been examined he is marked with a colored label—red for urgent surgery, blue for redressing, white for evacuation, each numbered 1, 2, or 3 in accordance with priority, and sent to one of the special wards—orthopedic, neurosurgical, thoracoabdominal, and lightly wounded. Each ward is equipped with its own x-ray, wound-dressing, and operating suite, and treatment by skilled specialists is instituted within 10 or 20 miles of the front line and within from twenty-four to forty-eight hours of wounding. The provision of every ward with theater and x-ray equipment may seem wasteful and extravagant; but it is to be recognized that each is a 200-bed ward, the equivalent of a small hospital which empties and refills every third or fourth day as patients are evacuated to the rear, and such a flow of casualties is more than enough to saturate one set of theater and x-ray equipment. This concentration of 200 wounded to a single ward is possible because patients are nursed on stretchers in tiers of two or even three, and laid on rods which are suspended from the upright supporting posts of the roof. The rods are easily turned back so that in periods of less intense activity only the middle bunks, or the middle and lower bunks, need be used, and sometimes the whole space may be cleared.

Such emergency hospital construction, with its emphasis on x-ray, plaster room, and operating-theater facilities rather than on ward design, was most impressive, particularly with regard to the speed of building which it permits, the conservation of space, the adaptability to a varying flow of casualties, the economy of transport of patients before and after operation, and the segregation and specialization which are possible almost at the line of battle. The principle of segregation is carried beyond the specialist wards of sorting-evacuating hospitals to specialist hospitals further behind the line of from 2,000 to 4,000 beds each. So great has been the flow of casualties that it has even been practicable to devote 2,000-bed hospitals to gunshot fractures of the thigh, to penetrating wounds of the hip joint, and to other special injuries.

CLOSED-PLASTER TECHNIQUE

The closed-plaster technique is used for all major wounds, compound fractures, and joint injuries. Prof. Yudin claims that in the surgery of war this was first practiced over ninety years ago by the famous Russian surgeon Pirogof.

"After the resection had been made, instead of amputation the limbs are put in plaster-of-Paris casts . . . but the main thing is that not all surgeons know how to apply a good plaster cast, the closed one . . . that is why I justified myself for applying closed and windowed plasters to every field knee wound. . . . I was surprised with the unacquaintance of the Italian and French surgeons with my method during the war of 1859. Neither the Frenchmen nor the Italians tried to apply the plaster. The worse it is for them."

Yudin teaches that after wound excision no tube or drain should be used, and no gauze pack or other "foreign body" should be inserted; an unpadded plaster cast is applied directly over the wound. I was interested to learn of this departure from the practice to which we are accustomed in this country, because I have always been impatient of discussion on the relative merits of vaseline gauze, plain gauze, and other forms of "pack." It is clear that in comparison with the principles of wound excision, immobilization, and freedom from repeated dressing, these are unimportant details of individual technique. But there is one essential difference of principle in the methods which are practised in Russia. "A large excision of all injured and all contused tissues" is recommended no matter how many hours or days have elapsed since wounding and "independently of the presence and degree of infection." In England we believe that free excision is indicated only during the first twelve, or possibly twenty-four hours, and that after that time wide dissection is liable to disseminate infection; we think that the correct treatment in late cases is incision and drainage rather than excision and drainage. When I submitted this contrary view Yudin maintained with all the dynamic force of which he is capable that no matter how acute and widespread the infection "simple incision and tamponade with gauze, or any kind of antiseptic, or vaseline by Winnett Orr, cannot replace the necessary excision of all damaged tissues and, still more important, the removal of foreign bodies. Such incisions are not a surgical aid, but only a primitive temporary measure in the most hopeless circumstances owing to enormous quantity of work. Such patients should be regarded as having undergone no surgical treatment at all."

Personally I am still unconvinced, but it is clear that further study is necessary. Large series of cases, comparable with Yudin's, with a similar proportion

of late, "malignant septical," and desperately ill patients, must be examined. The mortality must be compared with Yudin's figures (three to thirty days 4.1 per cent; after thirty days 1.3 per cent). The amputation rate must also be compared (6.5 per cent immediate amputations for vascular damage and gangrene, and 5.5 per cent late amputations for general septic condition).

JOINT WOUNDS

A similar principle is adopted by many surgeons in the treatment of joint wounds; resection of the joint is preferred to arthrotomy in both early and late cases. In the hip joint the head and neck of the femur are removed; in the knee joint the resected bone varies from a thin sliver to a large section of the femoral condyles, but always includes the joint capsule, without which drainage is considered inadequate. Sulfonamides are used and the limb is immobilized in plaster. On this subject there is some divergence of opinion, and arthrotomy of acutely infected joints has been advocated more recently in preference to resection. This coincides with our view. One of the striking features of the surgery of this war has been the excellence of function and the free mobility which are so often regained after the treatment of penetrating joint injuries by early excision of the wound (but not resection of the joint) and immobilization in plaster; we believe that resection at the height of acute infection is dangerous; and we think that excision of the head and neck of the femur leaves an unstable joint which is far less perfect in its function than a firmly ankylosed one.

CEREBRAL SURGERY

Surgeons in this country are already familiar with Burdenko's pioneer work in neurosurgery, with Proper Graschenko's clinical investigation into gas-gangrene infection of the brain, and with Lena Stern's physiological research on the blood-brain barrier and intracisternal injection. The main principles adopted in the treatment of craniocerebral wounds are: (1) serious cases are not to be operated upon until shock is controlled; (2) operation is to be deferred until skilled surgeons and equipment are available; expert investigation and operation two or three days after wounding is better than inexpert operations performed immediately; (3) hemorrhage and a rise of intracranial pressure are the only indications for operation on the spot; (4) the longest safe period of deferment is three days; after that time the operative mortality rises steeply; (5) specialized hospitals with neurosurgeon, neurologist, neuropathologist, ophthalmologist, otorhinologist, and radiologist must therefore be available within three days' travel of the battle line, and patients should usually travel by air at heights not greater than 5,000 meters; (6) patients with craniocerebral wounds stand evacuation better before than after operation; when operation has been performed the wounded man must stay where he is for from fifteen to twenty days; (7) in the diagnosis and location of cerebral abscess, contrast media are used, and excision with removal of the capsule is considered the treatment of choice.

BLOOD TRANSFUSION

The blood-donor system of Moscow is worthy of emulation throughout the world. In one hospital we saw 300 donors bled in a single day; in another there were no fewer than 600. Many thousand pints of plasma are also collected from filial institutes in other cities. Donors are assembled in different rooms in accordance with their blood groups, which have already been tested. They are given a special fat-free meal, undressed, and clad in sterile theater clothing, including caps, masks, and cloth boots. For each blood group there is a separate operating theater. A single woman surgeon with 2 nursing sisters and 5 technical assistants controls 6 operating tables simultaneously. The work is done with skill and precision. It is a model of careful organization, of the highest possible standard of theater asepsis, and of repeated check and control of both contamination and accurate blood grouping. Dried plasma is put up in small ampoules, connected by means of a rubber tube and clip to a larger ampoule of sterile distilled water, ready for immediate mixing and administration to the patient. Blood is flown to the front in thermostatic boxes, lined with glass wool and cork, with a central compartment for ice or warm water according to the season. At the regimental aid posts and field mobile hospitals the blood is stored in deep pits; the temperature is tested thrice daily, and in the summer months it is controlled by ice blocks which were stored underground after cutting in winter.

OTHER FIELDS OF SURGERY

So many aspects of surgery were studied that selection is difficult. One might write of ultrasonic emulsification of therapeutic agents, of intracarotid injection of sulfonamides, of intracisternal injection of antitetanic serum, of cap splints for maxillary fractures, of gap fractures of long bones, of acrylic resin for dentures (which are delivered many miles behind enemy lines), of plastic reconstruction of the penis by tube grafts and cartilage inlays producing an organ capable of both urination and erection, of the treatment of esophageal stricture by jejunal transplants, or of the excellent system of medical education by which 25,000 doctors a year are trained. The astonishing fact is that so high a standard of surgery has been achieved in a country where the full development is so young and where contacts with the surgery of other countries has been so limited.

We believe that Soviet surgeons would gain from visits to other countries; we believe that in this way their technique would be improved; but we believe with equal conviction that we gained from our visit to them. We did not approve of all we saw; we disagreed on the treatment of frost-bite; we were unconvinced of the merit of muds, balsams, and wood distillates; we thought that our rehabilitation

was better than theirs. But on the other hand much of their work is better than ours; their specialization is excellent; their training of medical students is more thorough; their organization of surgical services is superb. Each of us can learn from the other. In the words of Academician Burdenko: "Our friendship must be much tighter." (ORIGINAL ARTICLE)

ANTISEPTIC SURGERY; TREATMENT OF WOUNDS AND INFECTIONS

Mitchell, G. A. G., and Buttle, G. A. H.: Diflavine in Wound Therapy. *Lancet*, 1943, 245: 287.

Diflavine (2:7-diaminoacridine monohydrochloride) and proflavine (2:8-diaminoacridine sulfate) are less toxic than 5-aminoacridine hydrochloride. Diflavine powder has been used as a wound dressing in 47 cases and proflavine powder in more than 200 cases. Benefit was produced in almost every case. Most of the patients treated were battle casualties, and the lesions were of all grades of severity. The impression has been gained that diflavine is not quite as effective as proflavine. Diflavine and proflavine are active in vivo against streptococci, staphylococci, and clostridia. Diflavine is possibly also effective against the bacillus pyocyaneus.

J. M. MORA, M.D.

Robinson, C. N.: Treatment of Burns with Triple-Dye-Soap Mixture. *Lancet*, Lond., 1943, 245: 351.

A pliable, nonirritant antiseptic coagulum is needed for the treatment of burns in the field. Experiments have been carried out with gum acacia and triple-dye, egg albumin and triple-dye, collodion and triple-dye, soft soap and egg albumin, blood and soap, and triple-dye and soft soap. Of these, only the last three were satisfactory. Because of the difficulty of obtaining egg albumin, however, its use is not practicable at present.

A blood and soft-soap mixture makes a soft, durable, pliable coagulum under which healing seems to be rapid. Thus far, only 5 cases have been treated with this mixture.

A triple-dye and soap mixture produces a soft, fine, supple coagulum, which does not contract and which reduces sepsis. A group of 106 cases, mostly second-degree burns involving the face, hands, and other parts of the body, were treated with this mixture. Some of the burns were very extensive. Ninety-one of the cases were septic on admission, and 41 of these were febrile. There were no deaths, and no skin grafts were necessary; all of the burns healed in a satisfactory period with a minimum of scarring and contracture. SAMUEL KAHN, M.D.

Barnes J. M., and Rossiter, R. J.: The Toxicity of Tannic Acid. *Lancet*, 1943, 245: 218.

The toxicity of intravenous and intramuscular injections of tannic acid and sodium tannate was investigated in mice, rats, and guinea pigs.

Tannic acid and sodium tannate when injected intravenously were fatal to mice and guinea pigs in doses of 40 mgm. per kilogram. The fatal intramuscular dose, however, was considerably greater. For rats, sodium tannate proved to be more toxic when given intramuscularly than tannic acid.

After the intravenous and intramuscular injections of tannic acid, the internal organs of the animals gave a positive tannic-acid reaction. After the intravenous injection of tannic acid, mice sustained severe liver damage, as was observed histologically. The intramuscular injection of tannic acid or of sodium tannate, on the other hand, caused slight though very definite liver damage.

In the investigation of toxic effects resulting from the absorption of tannic acid from burned surfaces produced by the application of a 250 cc. beaker of hot water to the shaved skin, it was found that burns which covered a quarter of the body surface and which were treated with tannic acid had a higher mortality and resulted in greater loss in body weight than burns of the same extent in similar animals which were not treated with tannic acid.

After the application of tannic acid to large fatal burns, in which from one-third to two-thirds of the body surface was involved, the liver, lungs, kidney, and muscle beneath the burn gave a positive tannic-acid reaction. With smaller, nonfatal burns, involving only one-quarter of the body surface, the test was negative for the internal organs, but positive for the muscles lying beneath the burn. Moreover, the edematous fluid separating the muscles from the burned skin gave a positive reaction.

After the application of tannic acid to the raw area produced by burns measuring a quarter of the body surface, there was liver damage slightly greater than that seen in untreated animals similarly burned but not treated with tannic acid.

From these studies it is concluded that tannic acid when applied to a burned surface is absorbed and that its absorption is harmful, as evidenced by the increased mortality and weight loss which follows tannic-acid application. Furthermore, the histological appearance of the liver after the injection or application of tannic acid makes it probable that some of the ill effects following tannic-acid administration arise from liver damage.

This experimental evidence taken in conjunction with the fact that severe liver necrosis in human cases of burns has been reported only since the introduction of the tannic-acid technique, and then only when tannic acid was applied, strongly suggests that tannic acid should not be used indiscriminately, especially on large burned areas.

STEPHEN A. ZIEMAN, M.D.

Pulvertaft, R. J. V.: Local Therapy of War Wounds; with Penicillin. *Lancet*, Lond., 1943, 245: 341.

A number of cases of infected war wounds were treated with the calcium or sodium salts of penicillin and 15 of these are recorded.

Within twenty-four hours there was a uniform and almost complete drop in the number of gram-positive organisms, including clostridia, staphylococci.

streptococci, and corynebacteria. Gram-negative organisms were not affected. The therapeutic results were excellent. The solid drug was introduced into a cerebral abscess cavity without deleterious effect. A few experiments with penicillium-notatum culture filtrates, made locally, gave satisfactory results.

J. M. MORA, M.D.

Anglem, T. J., and Clute, H. M.: The Intraperitoneal Use of Sulfanilamide in Gastrointestinal Resections. *N. England J. M.*, 1943, 229: 432.

Immediately after the construction of an intestinal anastomosis, whether done by an open or a so-called "aseptic" technique, conditions exist that are most favorable for the effective action of sulfanilamide: The inoculum of bacteria along the suture line is small. If infection can be considered to exist at this time, it is presumably in a preinvasive stage and there is little or no protein digestion, and it may reasonably be assumed that antisulfonamide substances are not present in high concentration. By the local application of sulfanilamide along the suture line, an overwhelming concentration of the drug can be brought to bear on the small number of bacteria.

In the absence of any gross technical error, if local bacteriostasis along the suture line can be maintained long enough to permit the formation of a firm fibrin seal (which requires only a few hours), the danger of secondary leakage and peritonitis can be greatly diminished.

The authors used sulfanilamide by local implantation in 75 cases of gastrointestinal anastomosis. Their usual intraperitoneal dose was between 6 and 8 gm., with an additional 2 to 4 gm. placed in the wound. They had but one clear-cut toxic reaction—a toxic hepatitis, which occurred four days after a gastric resection but was followed by recovery.

The authors are convinced that the danger of a serious toxic reaction is slight when a single intraperitoneal dose of sulfanilamide is used, even when this dose is large.

In their series of 75 cases there was a mortality of 8 per cent. There were no deaths from peritonitis.

JOSEPH GASTER, M.D.

Robertson, M.: Gas Gangrene: Active Immunization by Means of Concentrated Toxoids. *Lancet*, Lond., 1943, 245: 311.

The three most important organisms causing gas gangrene are the clostridium oedematiens, clostridium welchii, and clostridium septicum, and the work described by the author concerns the infection of guinea pigs, separately with each of them. The purpose was to test the value of small doses of concentrated toxoids in immunizing the animals against infection with organisms corresponding to the toxoid.

The toxoids were in each case made from a single strain of high toxigenic capacity and derived from the supernatant fluid of cultures, the bacteria being discarded. They were toxoids in the strict sense of the word.

The organisms used for the infections were derived from strains other than those used in making the toxoids, except in the case of the clostridium welchii in which the homologous organism was used together with another pathogenic strain. The animals received an initial dose, followed, after an interval varying between ten days and three weeks, by a second dose; this constituted the primary immunization.

The duration and value of this procedure was explored in some of the animals. Others received a third dose after an interval of about eleven weeks. This additional dose, given at a period when the antitoxin content of the blood was found to have dropped considerably, caused a marked rise in the titer and inaugurated the secondary immunity, which was also tested by exposure to infection.

The authors conclude from their experiments that small doses of toxoid protected guinea pigs against the three organisms most frequently causing gas gangrene—the clostridium welchii, clostridium oedematiens, and clostridium septicum. Protection depends on the presence of an adequate amount of antitoxin in the circulating blood of the animal.

JOSEPH K. NARAT, M.D.

McIntosh, J., and Selbie, F. R.: Combined Action of Antitoxin and Local Chemotherapy on Clostridium-Welchii Infection in Mice. *Lancet*, 1943, 245: 224.

Experimental results clearly show that measures directed toward local clostridium-welchii infections are of great value, even when the infections have become generalized. Such measures should include full surgical toilet, followed by the application of a chemotherapeutic agent. Until more effective remedies are available, a finely ground mixture of 1 per cent proflavine in sulfathiazole should be used. This mixture is effective against the clostridium welchii, clostridium oedematiens, and clostridium septicum, the three main organisms causing gas gangrene, and has the advantage of diminishing the local toxic effects of proflavine, which are considerable when proflavine crystals are applied to healthy tissue in large amounts.

The results also emphasize the importance of early treatment. Whether the therapeutic measures are chemotherapy or serum therapy, or both, they should be initiated before serious deterioration of the tissue sets in, and the sooner they are initiated the better. In the experimental disease in mice, the limiting period appears to be four or five hours after the inception of the infection. The time factor is important in the treatment of anaerobic infections.

Antitoxin treatment combined with local chemotherapy is more effective than antitoxin or chemotherapy alone in the treatment of clostridium-welchii infection in mice.

SAMUEL KAHN, M.D.

Campiche, P.: The Present Status of Tetanus Prophylaxis. *West. J. Surg.*, 1943, 51: 359.

The author discusses the pros and cons of the value of tetanus prophylaxis. The general surgeons

have a tendency "to inject too often under peacetime conditions," while the industrial surgeons insist that tetanus is rare in their field of activity, and therefore many of them do not use the prophylactic injection because they think it unnecessary.

The fundamental factor of the whole problem is soil contamination. This conception of soil contamination, whether it is possible or probable, direct or indirect, immediate or remote, should be the deciding factor whether or not tetanus antitoxin is to be administered. J. M. MORA, M.D.

Shaffer, B., Lentz, J. W., and McGuire, J. A.: Sulfathiazole Eruptions: Sensitivity Induced by Local Therapy and Elicited by Oral Medication. *J. Am. M. Ass.*, 1943, 123: 17.

As a result of local sulfathiazole therapy, unfavorable reactions, some of them quite severe, may occur. Although the etiological agent in most cases of allergic contact dermatitis is readily demonstrated by appropriate patch testing, this does not appear to be the case in the majority of reports of "contact dermatitis" due to sulfathiazole. Efforts to elucidate the allergic mechanisms in sulfonamide eruptions of the toxic or systemic variety, such as those which follow the usual oral administration of these drugs, have met with failure.

A number of case reports are presented. Allergic studies and various techniques are described.

The dermatitis, instead of presenting the usual appearance of dermatitis venenata, tends to manifest itself as an exacerbation of the eruption for which the patient is being treated. Local application of sulfathiazole gives rise to generalized sensitization in the sense that subsequent oral administration of the drug may precipitate a sulfathiazole dermatitis. This eruption tends to imitate the condition for which the patient was originally treated; it begins and is more pronounced at the sites at which sulfathiazole was applied locally. It is believed that pyogenic sensitivity plays a major role in producing sensitizations of this type.

HAROLD C. OCHSNER, M.D.

ANESTHESIA

Rose, A. T.: Sodium Pentothal: Actual Experience in the Combat Zone. *Anesthesiology*, 1943, 4: 534.

This report is an account of the experiences of the 10th Evacuation Hospital with pentothal sodium used intravenously for anesthesia purposes.

A 2 per cent solution was used, and 30 cc. syringes were found most practical for the administration of the drug. A 6 in. length of rubber tubing, fitting from syringe to needle, gave freedom to the anesthetist for maintenance of the airway.

This drug was employed for practically every type of case with the exception of that presenting intra-abdominal disease, and for cases lasting as long as one hour or more. Morphine was given preanesthetically and also during anesthesia if the patient had a high pentothal tolerance.

The problem of the airway was discussed in detail. Those cases in which any difficulty with maintenance of an airway was anticipated, such as those involving surgery of the face, neck, or chest, or those requiring a prone position, were intubated under pentothal. Laryngospasm was prevented by the restricted use of the oropharyngeal airway, the adminstration of atropine or scopolamine in preanesthetic medication, and the maintenance of a sufficiently deep degree of anesthesia. When laryngospasm occurred during the course of surgical manipulation it was found that the best way to manage the problem was to cease the stimulation and increase the depth of anesthesia to such a point that the manifestation of the reflex would be prevented.

Emesis during pentothal anesthesia was best prevented by keeping food and drink from the patient for at least three hours before the scheduled time of anesthesia. However, when this was not possible, provisions were made for the contingency by having the head lower than the body and making certain that efficient suction was available for instantaneous use.

When venipuncture was found difficult or impossible, venesection or the sternal marrow route of administration was used. MARY KARP, M.D.

Case, E. H.: The Present Status of Trichlorethanol. *Anesthesiology*, 1943, 4: 523.

Interest in trichlorethanol was revived because of the difficulty in obtaining tribromethanol (avertin) and because of the similarity in action of the two drugs. The literature on trichlorethanol was reviewed, and a comparison of this drug with tribromethanol (avertin) was made.

Physically, trichlorethanol was found to be more stable and more easily measured than avertin.

Pharmacologically, it has a higher effective and toxic dose than does avertin. For equivalent doses there were no consistent differences between the respiratory or circulatory effects of the two drugs except that extra systoles were noted when trichlorethanol was administered intravenously. When fatal doses of either drug were given, the respiration failed before the heart failed. Hepatic function was found to be impaired to the same extent with each drug. Slightly more restlessness was encountered in dogs during the induction and emergence of the drug when trichlorethanol was used.

Two deaths were reported in the literature, 1 was in the 18th case and 1 in the 25th case. Both seemed to be cardiac in type. For this reason the author ran electrocardiographic tracings on dogs with damaged hearts. No abnormalities in the tracings were found.

The author showed experimentally that amylene hydrate in the amounts present in the avertin solution was not responsible for the depressant action of avertin, nor did it seem to affect the action of trichlorethanol when added to it.

Clinically, the drug was used in 30 patients. It was found that the effective dose was greater than that of avertin; individual variations in the response were considerable; the hypnotic action was as prompt

but not as lasting as that of avertin; and the decrease in blood pressure was definitely less.

The author concludes that trichlorethanol may be used interchangeably with avertin as a basal anesthetic. MARY KARP, M.D.

Parrett, V.: Caudal Anesthesia in 160 Obstetric Cases. *Am. J. Obst.*, 1943, 46: 417.

In this series of cases there were 581 deliveries, in which 160 patients, or 27.5 per cent, received caudal injections. The incidence of operative delivery (not including episiotomy alone) for the entire 581 cases was 19.6 per cent, while for the patients receiving caudal anesthesia the operative incidence was 36.2 per cent. This increased incidence of operative delivery was made up largely by cases in which outlet forceps and episiotomy were used.

Failure of the head to rotate necessitated operative aid in 15 cases, or 9.4 per cent. Taken month by month, the incidence of manual aid for failure to rotate has varied from 1 per cent to 4 per cent for the entire number of deliveries. This clear-cut increase in occiput-posterior presentations is probably due to the lack of "bearing down sensation" and accompanying expulsive effort, which added to the uterine contraction secure more forcible descent and subsequent rotation. Another factor is the relaxation of the levator-ani and perineal muscles which deprives the head of the "perineal scoop" that normally insures anterior rotation of the occiput.

Observation of the cases following delivery aided by caudal anesthesia reveals certain complications of varying degrees of severity. About half of the patients complain of tenderness on pressure over the sacrum, which they seldom note before palpation by the investigator. Tenderness over the sacrum occurs chiefly in cases in which entry of the canal was difficult. One case of respiratory failure was noted. This patient did not die.

EDWARD L. CORNELL, M.D.

Etherington-Wilson, W.: Specific Gravity of the Cerebrospinal Fluid in Spinal Anesthesia. *Brit. M. J.*, 1943, 2: 165.

The technique of spinal anesthesia with hypobaric solutions of nupercaine and spinocaine demands knowledge of the specific gravity of the cerebrospinal fluid in normal individuals and in pathological conditions, and also of the solution injected. If the specific gravity of these two solutions varies to any great extent the technique will not always be reliable. The specific gravity of the anesthetic agent (usually nupercaine) is known, but that of the cerebrospinal fluid is alleged to have markedly varied readings.

In a series of 314 cases of great variety, the specific gravity of the cerebrospinal fluid at normal body temperature, as measured with specific gravity beads, was found to remain constantly between 1.004 and 1.003, and was nearer 1.003. In spite of the pathological states which affect the cerebrospinal fluid there was no further variation in specific gravity of the fluid. ERNEST E. ARNHEIM, M.D.

SURGICAL INSTRUMENTS AND APPARATUS

Cohn, A. L., and Levitin, J.: Problems in Gastric Diagnosis: The Gastroscope as a Supplementary Aid to X-Ray Examination. *Gastroenterology*, 1943, 1: 841.

Much is expected of the roentgenologist, but it is known that 5 per cent of early carcinomas are not demonstrable roentgenologically. An ulcer can be demonstrated only if it penetrates the mucosa, consequently many acute ulcers are missed. There are no sure x-ray criteria for differentiating malignant from benign ulcers, malignant from benign growths, and intrinsic from extrinsic lesions; yet this differential diagnosis is most important. It is true, however, that the number of patients in whom a differential diagnosis is difficult is comparatively small. Any additional diagnostic aid, therefore, which will reduce this minimum of missed diagnoses is desirable.

Gastroscopy is a simple, safe procedure, and is a valuable aid to x-ray examination. A gross anatomical description of the gastric mucosa is made possible, and frequently information can be obtained which is not possible in any other way. Gastroscopy has been especially valuable in the diagnosis of mucosal lesions difficult or impossible to detect with x-rays. These are gastritis, granulomas, superficial erosions, and polyps. As a rule, gastroscopy gives more information in diagnosing gastritis than do x-rays.

Gastroscopy has both advantages and limitations. It is used to advantage in that group of cases in which the x-ray findings are doubtful or negative in the presence of gastric symptomatology, or when the x-ray findings do not correlate with the clinical findings. Not only is the percentage of correct diagnosis increased, but the viewing of the intact living organ gives a better understanding of the significance of many x-ray findings. Among the limitations of gastroscopy the following may be mentioned:

There are three blind areas in the stomach, namely, the lesser curvature of the antrum, the posterior wall near the cardia, and a small area of the midportion of the greater curvature. The instrument cannot safely be used when there are obstructive lesions of the esophagus, esophageal diverticula, mediastinal tumors, or aneurysms. It should not be used when there are esophageal varices. Again, it may be of no value in the presence of lesions of the deeper tissues in which there is no involvement of the mucosa.

Once an ulcer is demonstrated, a differential diagnosis is essential. In many instances the differentiation of the malignant from the benign ulcer can be made with x-rays alone. There are definite gastroscopic criteria to guide in the interpretation of malignant and benign ulcers.

A benign ulcer appears as a white or yellow, round or oval, smooth depression in an orange-red mucosal field. The edge may be sharp, or irregular, and readily distinguishable from the surrounding mucosa, which may be hyperemic and edematous, and at

times it may even overhang the crater. Folds are frequently seen converging toward the ulcer.

A malignant ulcer appears as an irregular depression in the center of an elevation. The floor is not smooth but irregular. The margin is not sharp and punched out; it may merge into the surrounding mucosa. The color of the floor is dead white, dirty gray, black-brown, or purple. Another sign recently described is the presence of a fine adherent froth probably due to a fermentative process. This froth is seen in the base of a malignant ulcer, but does not occur in benign lesions. The authors classify benign tumors arising from the gastric wall as leiomyomas, myomas, fibromas, adenopapillomas, lymphadenomas, neurofibromas, and hemangiomas. Some investigators have found that benign tumors formed 26 per cent of all gastric neoplasms. Leiomyomas are the most common of the benign tumors of the stomach.

On the roentgenogram the benign tumor appears as a well rounded, circumscribed translucent area in the barium-filled stomach wall. Consequently, the mucosal folds about the tumor are intact and peristalsis is present.

The carcinoma, which is the most frequent of all tumors of the stomach, shows as an irregularly outlined translucent area in the roentgenogram. There is invasion of the stomach wall resulting in rigidity, loss of peristalsis in this area, and an abnormal mucosal pattern. The lumen of the stomach becomes narrowed.

The supplementary aid which gastroscopy is called upon to give is not in the differential diagnosis of benign tumors, but in the differentiation between a benign and a malignant tumor. This is readily done in the majority of cases.

The extent of a malignant lesion cannot be judged by the x-ray appearance. Very frequently gastroscopic examination will show a greater involvement than appears on the film. Gastroscopic examination makes it possible that carcinoma can be diagnosed and classified, and that the extent of involvement can be determined before surgery. Hence it is possible to give an estimate of the prognosis and operability.

Polyps, which are rarely diagnosed with x-rays, can be visualized by gastroscopy and their extent determined. Necrosis of polyps may be detected early. If, as is now agreed by some, a large polyp in atrophic mucosa should be considered a precancerous lesion, its early detection is of the utmost importance.

The cause of gastric hemorrhage can be determined by means of the gastroscope, which determines whether it is surgical or nonsurgical. The roentgenologist is frequently called upon to investigate an unexplained gastric hemorrhage. The bleeding may be due to superficial ulcerations which cannot be demonstrated with x-rays but can readily be seen by means of a gastroscope. The bleeding may be the result of nonsurgical conditions such as gastritis, duodenitis, degenerative vascular conditions of old people, hypertension with congestion of the stomach wall, renal insufficiency, heart failure, mitral stenosis, leucemia, anemia, and cirrhosis of the liver. Cases of bleeding requiring prompt surgical treatment are papillomas, carcinomas, and ulcers in benign tumors. A differential diagnosis between a surgical and nonsurgical condition is important.

Persistent spasm of the antrum taxes the diagnostic acumen of the roentgenologist more than any other finding. The spasm may be due to an intrinsic or an extrinsic lesion, or to a nervous disturbance. An abnormal distribution of sympathetically innervated prepyloric muscle fibers may give the spasm a simulating filling defect. If the mucosal folds of the antrum can be demonstrated as intact, a lesion in this location can be eliminated and the cause of the spasm must be sought elsewhere. Spasms due to a nervous disturbance may be effaced with antispasmodics.

A common cause of error in x-ray diagnoses in this region is the change produced by chronic gastritis simulating carcinoma. This is due to the fact that a narrowed pylorus and polypoid excrescences occur in this disease.

Within the stomach an ulcer on the lesser curvature will often cause spasm of the antrum. Spasm has also been found with a carcinoma of the cardiac end of the esophagus.

Outside of the stomach, gall-bladder disease, duodenal ulcer, and a diseased appendix may cause an antral spasm. Psychic influences can give the same picture reflexively. The deformed antrum may be caused by a lesion in the pancreas.

The correct diagnosis of an antral lesion is most important to the patient, since the antrum is a favorable site for malignancy and the need of surgery. Therefore the supplementary aid which gastroscopy can give in this problem is most important.

Gastritis, both the hypertrophic and atrophic types, can be diagnosed only by gastroscopy. The gastroscopic picture of chronic hypertrophic gastritis varies with the location, degree, and extent of the disease. The most common site of the lesion is the body of the stomach, the antrum being affected less frequently. In the early stages the mucosa is swollen, dull, and velvety in appearance, the normal glistening highlights being diminished. As the hypertrophy progresses, the mucosa, especially in the body of the stomach, takes on the appearance of small elevated areas of varying size. Still later these areas appear as small or large nodules.

The patients with the "postoperative stomach" live to plague the gastroenterologist and the roentgenologist. Many have a large functional overlay, but some have recurrences of their ulcer or a new ulcer at the site of the enterostomy, or just below it in the jejunum. The gastroscopist can diagnose lesions such as marginal ulcers and gastritis following operation. He can also differentiate the distorted folds of the postoperative stomach from an ulcer.

The article is presented in a clear, straightforward manner and is replete with excellent illustrations.

MATHIAS J. SEIFERT, M.D.

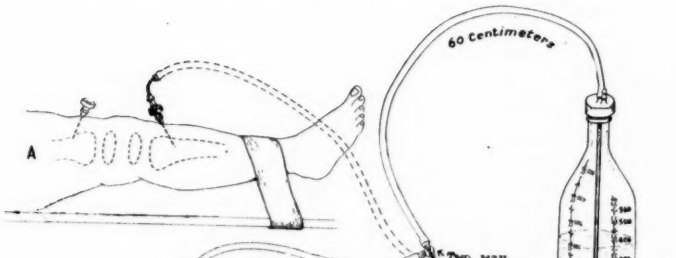

Fig. 1. Convenient arrangement for the rapid injection of substances (A) in the bone marrow of the tibia (or femur) of children under three years of age or (B) in the sternum of adults. All connections must be tight. (C) Convenient sizes of the needle generally used in infusions via the bone marrow. Metal adapters and metal tip syringes are preferable, to avoid glass chipping.

Tocantins, L. M., Price, A. H., and O'Neill, J. F.: Infusions Via the Bone Marrow in Children. *Pennsylvania M. J.*, 1943, 46: 1267.

Citrated blood, plasma, physiological solution of sodium chloride, and 5 per cent glucose solution have been infused through the marrow of the tibia or femur of 52 infants, in whose treatment intravenous infusions were considered urgent, but difficult or impossible.

Seventy-nine such infusions were done. With the exception of minor local reactions, no local or constitutional reactions occurred, as disclosed by clinical and x-ray examination as late as twenty-one months after the infusions.

A prompt cessation of bleeding followed the transfusion of blood through the marrow of the tibia in a hemophilic infant.

The upper third of the tibia and the lower third of the femur are the sites of choice for intramedullary infusions in infants. Under no circumstances should the sternum be used in infants three years of age or less. Enough marrow should be removed by aspiration to make certain that the needle is properly located. No material should be injected or infused until marrow is clearly obtained.

A detailed description of the technical steps and apparatus for infusion through the bone marrow has been given previously. SAMUEL KAHN, M.D.

PHYSICOCHEMICAL METHODS IN SURGERY

ROENTGENOLOGY

Steinberg, M. F., Grishman, A., and Sussman, M. L.: Angiocardiography in Congenital Heart Disease. Patent Ductus Arteriosus. *Am. J. Roentg.*, 1943, 50: 306.

Since surgical ligation of patent ductus arteriosus has been proved feasible and successful, the need for accurate diagnosis of this condition is highly desirable in order that the indication for surgical intervention be better established. Roentgen findings, while helpful, are not pathognomonic. The authors have studied 27 such cases by means of angiography and these cases form the basis of this report. They are tabulated as to the age and sex of the patient, his age at the discovery of the cardiac lesion, and the symptoms, physical findings, clinical complications, blood pressure, electrocardiogram, phonocardiogram, roentgen examination of the heart, angiocardiography, operation, size of the ductus arteriosus, and remarks.

Consideration is given to the anatomical and physiological aspects of the condition. The technical factors used in the angiocardiographic studies are described briefly. The findings revealed are discussed in detail. In the case of isolated patent ductus arteriosus the following are noted:

1. A distinct localized dilatation of the descending aorta just beyond the isthmus which varies in size and shape from a localized bulge to a uniformly dilated segment. The appearance may be due either to the infundibulum of the patent ductus or perhaps in some cases to a traction aneurysm of the aorta.
2. An elevation of the main and left pulmonary arteries, the appearance suggesting that they are drawn toward the isthmus of the aorta.
3. Moderate to marked dilatation of the pulmonary artery. This usually found, but was absent in 25 per cent of the cases.
4. Varying degrees of left ventricular dilatation.

Of 27 cases of patent ductus arteriosus (12 of which were proved at operation) 26 showed the aortic abnormality described.

The differential diagnosis of congenital lesions which in the authors' experience have been mistakenly diagnosed as patent ductus arteriosus is discussed briefly, and it is stated that the aortic abnormality described with elevation of the pulmonary artery was found only in patent ductus arteriosus.

A. HARTUNG, M.D.

Hatchette, S.: Roentgenological Diagnosis of Left-Sided Appendicitis. *Am. J. Roentg.*, 1943, 50: 244.

It is believed that a diagnosis of left-sided appendicitis, made entirely by roentgenological means and confirmed by surgical operation and pathological examination, is sufficiently rare and of enough interest to warrant reporting. This case, which is reported in detail, showed an incomplete rotation of the colon which was not discovered until the roentgenological examination was made. All of the other viscera were normally located. The pain of which the patient complained was located in the left side of the abdomen just above the level of the anterior iliac spine. There was no pain or tenderness in the right lower quadrant. Clinical examinations by a competent internist and a competent surgeon had led both to suspect a diverticulitis, and the patient was referred for roentgenological examination of the colon with a presumptive diagnosis of "diverticulitis."

Fig. 1. Enlarged view of appendix showing filling defect at the tip.

The embryology of anomalous rotation of the colon is given brief consideration. Hembrow's classification of left-sided appendices is cited and his explanation of the location of the pain associated with inflammation occurring in the different types is given. LeWald's figures of the incidence of left-sided appendices are mentioned, and Nix and Nix are quoted to the effect that "left-sided appendicitis, according to Walther, occurs once in every 1,000 cases."

The explanation for left-sided pain which occurs in some cases of left-sided appendicitis, and which has been ascribed to various causes by others, is explained by the author as being due to adherence and

involvement of the mesentery of the left side of the abdomen in an inflammatory process originating from the appendix. A. HARTUNG, M.D.

Jenkinson, E. L., and Brown, W. H.: The Differentiation of Endometriosis and Carcinoma of the Sigmoid Colon. *Minnesota Med.*, 1943, 26: 773.

Early diagnosis of colon malignancy is important to both the patient and physician. Approximately 70 per cent of all colon surgery is for carcinoma. In 369, or 68 per cent, of 542 operations on the colon, Rankin found carcinoma. Functional or organic lesions in one part of the gastrointestinal tract may readily cause disturbances in other regions. For this reason, emphasis should be placed on complete intestinal studies, including colon and gall-bladder examinations.

Although the differential diagnosis of inflammatory and malignant lesions of the colon (particularly of the sigmoid) has been repeatedly stressed in the literature, practically no reference has been made to endometrial lesions which produce a constriction similar to that of carcinoma.

Endometriosis of the colon occurs in women during active menstrual life, between the ages of twenty-five and forty-five years. One hundred and seventeen cases were reviewed during the period from 1939 to 1941. The consensus is that 15 per cent of all women develop pelvic endometriosis during their active menstrual life, and of these, 25 per cent have lesions of the rectosigmoid.

Constricting lesions of the sigmoid colon are intrinsic or extrinsic, and malignant or inflammatory.

Intrinsic carcinoma generally occurs in patients over forty years of age. Pertinent symptoms are: a change in bowel habits, constipation, red blood in the stool, and a mucous discharge. Proctoscopic examination may reveal the tumor. Roentgen findings are: short constant filling defects (not more than from 1 to 2 in. in length), well defined margins, irregular walls, involvement of the mucosa, and slight fixation or tenderness.

Intrinsic inflammatory processes occur in any age group. Symptoms may persist for years and the chief complaint is a dull pain in the abdomen. Bloody diarrhea is present in cases of colitis. The diagnosis is made by means of bacteriological examinations, the presence of gross blood, mucus, pus, and specific organisms. Roentgen findings are: inconstant long constriction (from 4 to 6 in.), margins ill defined and irregular, and in some cases exquisite tenderness.

In extrinsic malignancies there are no characteristic symptoms or findings.

Extrinsic inflammatory lesions (endometriosis) occur in women usually between twenty-five and forty years of age, with a high incidence of menstrual abnormalities. Patients may complain of progressive obstruction which is exacerbated during the menses. A history of previous surgery is of diagnostic help. Roentgen findings are: a short, inconstant defect (from 2 to 4 in. long), regular and well demarcated borders, intact mucosa, and marked fixation and tenderness. Smaller implants may be present.

The authors stress the importance of a careful history and utilization of all diagnostic methods in the differentiation of endometriosis and carcinoma of the sigmoid colon. MAURICE D. SACHS, M.D.

Mark, J.: Venography. *Ann. Surg.*, 1943, 118: 469.

The technique of venography and a simple modification is described by the author. The technique advocated by Bauer and others is as follows:

A 2 cm. incision is made behind the lateral malleolus. The lesser saphenous vein is isolated and the distal portion is tied with fine silk. A cannula is inserted into the proximal portion of the vein. Twenty cubic centimeters of 35 per cent diodrast are injected over a sixty-second period and as the last few cubic centimeters are injected roentgen exposure is made on a 14 by 17 film. By use of this method, the vascular system of the leg and distal thigh are visualized. Following the injection, the cannula is removed; the vein is tied; the tissue is lavaged with saline solution to remove any residual dye, and the skin is closed with silk suture.

The author eliminates the necessity of incision by using a venopuncture into a superficial vein. The deep venous veins are visualized better if the patient is placed in an exaggerated Trendelenberg position. No undue reactions were observed following the use of diodrast.

Nine cases are presented which illustrate the value of venography. One case was that of Buerger's disease with dilatation of the deep veins, splintering of the intima, and multiple defects caused by thrombi.

This technique is invaluable in contemplated surgery when a complete, preliminary, anatomical picture of the vascular bed can be obtained. It is also of diagnostic help in cases of leg swelling with pain, and with or without varicosities.

MAURICE D. SACHS, M.D.

Pohle, E. A., McAney, J. B., and Lovell, B. K.: Radiation Therapy in Carcinoma of the Rectum and Sigmoid. Experimental Study of the "Danger" Dose of Roentgen Rays for the Intestinal Mucosa in Dogs and an Analysis of 195 Cases Treated at the State of Wisconsin General Hospital During the Period from 1928 to 1938. *Radiology*, 1943, 41: 225.

Radiation therapy is a valuable adjunct to surgery in the treatment of carcinoma of the rectum as clinical and experimental studies have shown that the rectal mucosa is radiosensitive. However, ulceration and even perforation of the mucosa have been observed not infrequently.

In order to determine the tolerance dose of the rectal mucosa, radiation therapy was administered to 9 dogs averaging 10 kgm. in weight and 9 cm. in pelvic diameter. The factors were as follows: 175 kv., 15 ma., 0.5 mm. of copper plus 1 mm. of aluminum filtration, 50 cm. F. S. D., and output 40 r/min. With one anterior and one posterior

10 by 10 cm. field, 600 roentgens were given to 2 dogs in a single dose. Nine hundred roentgens per port were given to 2 other dogs, and 1,200 roentgens per port to 3 other dogs.

Over a period of thirty-one months, it was found that the degree of symptoms and radiation proctitis varied with the dosage. One animal died from peritonitis with no demonstrable perforation. Another died from perforation ten weeks after irradiation. All 3 dogs who received 1,200 roentgens died of intestinal perforation and ulcerations. A fractional dose was given to 1 dog (360 roentgens per port daily for seven consecutive days). The reaction of the intestinal mucosa in this dog was much milder. The authors concluded that dogs cannot tolerate a single dose above 1,300 roentgens, and that the reaction seemed to be reduced when the fractional method was used.

From 1928 to 1938, 195 cases of carcinoma of the rectum and sigmoid were reviewed. One hundred and twenty-three were in males and 72 in females. The age group in the majority was between fifty and seventy years. Rectal bleeding was present in 68 per cent of the cases; pain, diarrhea, and constipation in from 30 to 40 per cent, and obstruction in 7 per cent. The rectosigmoid junction was the site most commonly involved. One hundred and seventy-seven cases had some form of surgery. Exploratory laparotomy revealed local extension or metastases in 110 cases. Fifty-four cases were considered operable and radiation therapy was given postoperatively. Most of the 54 cases were in stage 2 or 3. Twelve other cases were rendered suitable for surgery following irradiation. Colostomy followed by x-ray therapy was done in 96 cases; 17 of these also received interstitial radon seeds.

Cases receiving radiation therapy were individualized and roughly divided into four groups: inoperable, borderline operable, postoperative and recurrent, and metastatic. One hundred and four inoperable cases were given palliative therapy and 50 per cent showed subjective improvement for periods of from three to seven months, while 5 per cent were improved from one to three years. Twenty per cent remained stationary or regressed in from three to twelve months. Four per cent remained stationary or regressed in from one to three years. Thirty-four per cent did not benefit from irradiation. There were 12 borderline cases of which 3 terminated fatally following surgery and the remainder developed recurrences in periods varying from six to forty-eight months. There were 54 operable cases of which 26 did not develop recurrences over a nine-year period, while 27 developed recurrences in from three months to three years. There were 24 recurrences or metastatic cases treated and followed up for from three to six months. Twelve patients were benefited by the irradiation.

The authors are of the opinion that radiation therapy is of definite value in rendering a borderline carcinoma operable and that it is a good palliative agent when it is used in the treatment of recurrent carcinoma or metastases.

MAURICE D. SACHS, M.D.

MISCELLANEOUS

CLINICAL ENTITIES—GENERAL PHYSIOLOGICAL CONDITIONS

Noth, P. H., and Loew, E. R.: The Colloidal-Gold Reaction of Blood Serum in Hepatic and Other Diseases. *Am. J. Digest. Dis.*, 1943, 10: 348.

Studies of the colloidal-gold reaction were made on the blood serum of 245 patients with and without hepatic disease, and on the blood serum of 25 normal males. In addition, bromsulfalein and hippuric-acid excretion tests, and icteric-index determinations were made on most patients. Frequently each test was repeated during the course of the disease.

The colloidal-gold test was positive in 27 of 30 patients with hepatic cirrhosis. There were only a few instances in which the results of the various indices of hepatic function did not agree. The authors explain this uniformity as being partially due to the advanced stage of the hepatic disease. Improvement in hepatic function, indicated by the bromsulfalein or hippuric-acid test, was usually apparent in the physical condition of the patients, as well as in the levels of serum protein, hemoglobin, and erythrocytes. In no instance did the serum colloidal-gold test return to normal.

Colloidal gold reactions were positive in 22 of 29 cases of acute and subacute hepatitis, on either the first or subsequent tests. Hippuric-acid tests were positive in 8 of 13 of these cases. There were only two reversals of a positive to a negative colloidal-gold reaction as the patients recovered.

The colloidal-gold test was originally negative in 5 cases, and positive in 1 case of obstructive jaundice. In 2 cases in which it was originally negative it became positive. This test was positive in 7 of 11 cases of primary and metastatic carcinoma of the liver. Among the 4 cases with negative tests there was 1 positive and 1 negative for the bromsulfalein test, and 1 positive for the hippuric-acid test.

The test was positive in 2 cases of acute tuberculous hepatitis, and negative in 1 case of generalized miliary tuberculosis. It was negative in a case of severe lipoidosis of the liver in which the bromsulfalein test was positive. This test was positive in 8 and negative in 23 cases of hepatomegaly due to cardiac failure.

A positive colloidal-gold reaction occurred in only 1 of 21 cases of acute and chronic cholecystitis. The test was negative in 76 of 90 patients with no clinical or usual laboratory evidence of hepatic disease, and it was negative in all of the 25 normal males. Of the 14 cases with positive reactions among the 90 cases of nonhepatic disease, 7 presented syphilis and 4 presented fever of long duration.

In correlating the test with the autopsy findings it was occasionally positive when other tests were negative, and the reverse situation occurred also.

EARL O. LATIMER, M.D.

Apter, L., Hull, E., and Adams, C. C.: Maintenance of the Sedimentation Rate as a Test for Malignant Disease. *Am. J. M. Sc.*, 1943, 206: 168.

The speed with which erythrocytes in citrated or oxalated blood settle is retarded if the blood is allowed to stand for several hours before the test is set up. To determine if the reports of other authors, to the effect that this retardation is absent in malignant disease, could be of diagnostic value, Apter, Hull, and Adams determined the sedimentation rates in a number of patients in whom the presence or absence of malignant disease had been established. This was done immediately after the withdrawal of the blood and also after it had been stored, and in this way they attempted to evaluate the comparative sedimentation rates as a test for malignant disease. Standard tests were employed, and the temperature of the blood during storage and during the tests was controlled. This was necessary because it was shown that the retardation or maintenance of the initial sedimentation rate depends in a large part upon the temperature of the blood when the rates are determined and at which it is stored.

Only one set of temperature circumstances was found at which there was significantly less retardation of the sedimentation rate in cancer than in nonmalignant diseases. When the blood was stored twenty-four hours at 10° C. and the rates were determined with the blood at the same temperature, the rate remained within 20 per cent of the initial rate in about 4 of 5 cancer cases, and decreased more than 20 per cent in less than half of the cases of nonmalignant disease.

Thus, the test is far from reliable, is empirical, and is not at all related to the presence of cancer, and cannot be correlated with any known differences between the blood cells or plasma of persons with and without cancer. The authors conclude, "By the methods which we used, maintenance of the initial sedimentation rate in blood stored for 24 hours was not a reliable criterion for the presence of malignant disease."

EDWIN J. PULASKI, M.D.

Ariel, I., Abels, J. C., Pack, G. T., and Rhoads, C. P. Metabolic Studies of Patients with Cancer of the Gastrointestinal Tract: The Treatment of Hypochloremia Refractory to the Administration of Sodium Chloride, Especially in Patients with Gastrointestinal Cancer. *J. Am. M. Ass.*, 1943, 123: 28.

Immediate postoperative disturbances of the water and electrolyte balance usually are corrected promptly by the adequate administration of isotonic solution of sodium chloride. Some instances of postoperative hypochloremia, however, are refractory to that procedure. Usually attention is first directed to these patients because of their lethargy, anorexia, nausea, and increasing abdominal distention. Blood

studies reveal hypochloremia, alkalosis, and hypoproteinemia. The intestine gradually becomes inactive. Flat roentgenograms of the abdomen are consistent with the picture of intestinal obstruction, and at laparotomy edema of the intestine is found. The symptoms of fluid retention appear to be localized to the gastrointestinal tract and lungs, and only after the administration of considerable saline solution (in an attempt to counteract the hypochloremia) does peripheral edema appear.

Since the fluid and electrolyte balance of the organism is connected intimately with the concentrations of protein in the serum, it was conceived that the hypoproteinemia rendered the attempts to treat the hypochloremia by isotonic saline solution ineffectual. If this should be the case, treatment of the altered electrolyte equilibrium should include measures to raise the protein levels. Accordingly, 4 patients (in the Memorial Hospital for the Treatment of Cancer and Allied Diseases, New York), who manifested the syndrome described after operation for cancer of the gastrointestinal tract, were given orally or parenterally large amounts of protein in addition to adequate amounts of fluid and sodium chloride. In each instance the symptoms were relieved, and the serum proteins, chlorides, and the carbon-dioxide combining power were restored to normal. ERNEST E. ARNHEIM, M.D.

Nathanson, I. T.: Medical Progress: Cancer: Results of Treatment. *N. England J. M.*, 1943, 229: 468.

There is now striking and convincing evidence that cancer in its various manifestations can be cured. This report deals with the probability of cure of the most common forms of neoplastic disease. The author reviews the major contributions to the literature on this subject and analyzes statistics from the large clinics throughout the world. These are summarized in Table 1.

Clinical freedom from demonstrable disease has been accepted as the criterion of cure. Authorities throughout the world have agreed generally to accept an arbitrary period of five years of freedom from disease as representing a clinical cure, although in certain cancers a shorter period is reliable and in others a longer period is necessary.

Cancer of the skin is usually easily detected and amenable to therapy by any of the accepted methods; consequently its rate of curability is high.

Most of the figures concerning cancer of the breast deal only with operable lesions. The prognosis for all cases of cancer of the breast probably would be lower. It is generally agreed that the radical breast resection is the procedure of choice and should be performed whenever possible.

The degree of curability in cancer of the oral cavity and respiratory tract varies with the site of the primary lesion. The end-results for cancer of the lip include only those lesions that arise on the mucous membrane. The lesions of the buccal mucosa comprise only those which arise from the inside of the

TABLE I.—REPORTED FIVE-YEAR CURABILITY RATES IN COMMON TYPES OF MALIGNANT NEOPLASM.

Organ or Type		Curability Rate Per Cent
Skin		48–68
Basal cell	38–74	
Epidermoid	39–56	
Breast:		
Absolute		22–28
Relative		30–51
Oral cavity:		
Lip		59–70
Buccal mucosa		26–31
Gingivae		27
Lower	15–60	
Upper	33–74	
Palate		23–38
Hard	44*	
Soft	20*	
Tongue		14–37
Floor of mouth		18–32
Tonsil		15–32
Respiratory tract:		
Pharynx:		
Nasopharynx		18–30
Mesopharynx		15
Hypopharynx		6–12
Larynx:		
Operable:		
Laryngofissure (early cases)		80
Total laryngectomy		55
Inoperable		27
Thyroid gland:		
Early cases		70
All types		26
Gastrointestinal tract:		
Stomach:		
Absolute		5
Relative		15–30
Colon:		
Absolute		29
Relative		38–81
Rectum:		
Absolute		25
Relative		38–73
Urinary tract:		
Bladder		16–55
Kidney		19–33
Male genital tract:		
Penis		35–40
Testicle		15–53
Prostate:		
All cases		8
Operable		50–58
Female genital tract:		
Vulva		26–32
Vagina		30
Cervix		20–40
Endometrium		35–45
Operable (surgery)	48–70	
Operable and inoperable (radiation)	35–45	
Ovary		16–35
Sarcomas:		
Malignant melanoma		22–42
Fibrosarcoma		18
Osteogenic sarcoma		19–39

*Three-year rate.

cheek. Cancer of the gums refers to those lesions which have their site of origin in the mucous membrane overlying the upper and lower alveoli. The curability rate for cancer of the tongue is better for lesions of the anterior portion than for those of the posterior portion. Lesions of the tonsils and pharynx generally have low curability rates because they frequently are not recognized until swelling in the neck indicates the presence of lymph-node involvement. Intrinsic carcinoma of the larynx tends to remain confined to the larynx, is operable, and has a relatively high curability rate. Lesions which extend beyond the larynx or arise in the hypopharynx are seldom amenable to surgery.

Cancer of the thyroid gland is frequently discovered after thyroidectomy for other reasons. The prognosis is altered by the frequency of blood-vessel invasion, lymph-node metastases, and spread to distant organs.

Cancer of the gastrointestinal tract, if seen in the operable stage, is a curable disease. Approximately one-half of all patients with cancer of the stomach are operable, but, unfortunately, only about 50 per cent of these are suitable for radical curative surgery.

Operability rates in cancer of the colon are good. The site of the lesion affects the curability rate. Lesions of the right colon have a five-year survival rate of from 51 to 71 per cent. Lesions in the transverse colon have a survival rate of about 40 per cent, and in the left colon of about 38 per cent.

Cancer of the rectum now has an operability rate of from 50 to 75 per cent and a mortality rate of from 7 to 13 per cent. The former has increased and the latter decreased.

Curability figures for cancer of the urinary tract, as for cancer elsewhere, vary with the type and extent of the disease, the grade of malignancy, and the degree of radiosensitivity and operability.

Patients with cancer of the male genital tract seldom present themselves for treatment early in the disease; thus the curability figures are rather poor.

Lesions of the female genital tract differ in histological type, in radiosensitivity, and in accessibility for treatment by irradiation or surgery, and treatment for each lesion is modified by these conditions.

The control of sarcomas is difficult because of their tendency to metastasize through the blood stream, and their curability rate is, in general, low.

In conclusion, the author urges that more uniform and complete methods of reporting results be adopted, so that series of cases from each clinic can be compared directly. In this way more efficient therapy may be obtained.

EDWARD W. GIBBS, M.D.

Katz, S., Cake, C. P., and Reed, H. R.: Sarcoidosis. *N. England J. M.*, 1943, 229: 498.

The authors report 10 cases of sarcoidosis and state that the condition (also called benign lymphogranuloma) is now recognized to be a generalized disease that may involve any organ in the body and thereby give rise to many clinical syndromes.

The cause of sarcoidosis is not clear. Many pathologists believe that it is a benign form of tuberculosis, basing this concept on the histological similarity between the two conditions, the occasional recovery of tubercle bacilli, and the reported cases of termination in frank tuberculosis. Against this concept are the facts that tubercle bacilli usually cannot be demonstrated by culture or animal inoculation, and that from 60 to 80 per cent of cases fail to show positive skin reactions to tuberculin. The proponents of the theory explain this by an atypical or nonacidfast phase of the bacillus. Several reports give support to the theory that sarcoidosis is due to an atypical tubercle bacillus and that its peculiar manifestations are due to lack of tuberculin allergy.

According to Filho, the entire sarcoid syndrome may be found in leprosy, including skin lesions, bone changes, lymphadenopathy, and anergy to tuberculin.

The presence of eosinophils in the blood stream in some cases suggests an allergic state. The fact that neutropenia and leucopenia may be found in the disease suggests that a virus is the etiological agent.

Clinically, sarcoidosis is characterized by widespread involvement of one or more organs, with few constitutional manifestations. The disease begins insidiously in early adult life or childhood and usually pursues an indolent course. The diversity of its clinical forms is explained by the association of lesions in multiple organs. Contrariwise, seldom are all the organs involved in the same patient. The skin lesions are of several types: painless; nonpruritic; presenting violaceous plaques with no surrounding erythema or induration, which occur most frequently on the face, arms, and legs, but at times are widespread; presenting localized nodules, most commonly involving the eyelids, nares, fingers, and ears; and combinations of the two last types. Destruction and distortion of the nares may occur. The nails may be striated and brittle, and the nail beds often show the lesions. The oral and nasal mucosa may be involved. The most common initial finding in sarcoidosis is enlargement of the superficial lymph nodes. The adenopathy may be limited or generalized, and varies considerably in degree. The nodes most frequently involved are the preauricular, postauricular, submaxillary, submental, and epitrochlear. Lymph nodes along the course of the major lymphatic vessels in the arm may be palpable, and those of normal size or only slightly enlarged may show a typical sarcoid lesion. Pulmonary lesions are common. Bone lesions occur in from 10 to 20 per cent of the cases, usually involving the phalanges, metacarpals, and metatarsals. However, the tarsal and carpal bones and occasionally the long bones may be affected. Circumscribed cysts without change in the density of the surrounding bone represent the usual type of involvement. The lesions are chronic and may resolve or progress irregularly. They do not perforate and form fistulas, but there may be inflammation and tenderness of

the overlying tissues. Deformities, and even painless mutilation of the fingers such as occur in leprosy are seen. X-ray examination of the bones is rarely positive in the absence of some obvious deformity.

Because of the fact that groups of organs may be involved in almost innumerable combinations, a great variety of clinical syndromes result. It is to be noted, however, that all the extracutaneous lesions are characterized by their latency and their tendency toward spontaneous regression, in contrast to the much more chronic behavior of the skin lesions.

The laboratory findings, although not constant, may be of aid in supporting the diagnosis. Anemia is not often present. The white-cell count is usually normal or below normal. Marked leucopenia suggests splenic involvement, whether or not the spleen is palpably enlarged. The only abnormality of any significance noted during the differential count is eosinophilia; some cases, however, never have it, whereas in others it is transient. The plasma proteins show an interesting variation. The globulin fraction is commonly elevated sufficiently to raise the total plasma protein.

Sarcoidosis is characterized by a chronic, usually benign course and periods of remission. Complete cure may occur. The prognosis is good, and the disease is usually not fatal except when vital organs are involved.

Sarcoidosis must be differentiated from Hodgkin's disease, lymphosarcoma, bronchiolitis fibrosa obliterans, erythema nodosum, leucemia, fungous infection, tuberculosis (especially the noncaseous variety) and syphilis. The correct diagnosis is usually made by exclusion or biopsy.

Various types of treatment have been advocated. Arsenicals, iodides, leprosol, tuberculin, hyperpyrexia, gold salts, roentgen rays, and radium have been used without great success. Carbon-dioxide snow and x-ray therapy have, however, been of some value in the treatment of skin lesions. It is difficult to evaluate any form of therapy in view of the natural tendency of the disease to undergo spontaneous remission. Until more is known of its cause and pathogenesis treatment must remain empirical.

JOSEPH K. NARAT, M.D.

GENERAL BACTERIAL, PROTOZOAN, AND PARASITIC INFECTIONS

Moore, M., Cooper, Z. K., and Weiss, R. S.: Chromomycosis (Chromoblastomycosis). *J. Am. M. Ass.*, 1943, 122: 1237.

The authors report 2 cases of chromomycosis (chromoblastomycosis) or dermatitis verrucosa. These 2 cases are the eighth and ninth cases to be reported in the continental United States.

The lesion in the first case was of five years' duration and was located on the left wrist. It was verrucous and granulomatous and was difficult to differentiate clinically from tuberculosis verrucosa cutis, syphilis, granuloma annulare, porokeratosis, and blastomycosis. The microscopic features of the lesion had all of the characteristics of a granulomatous lesion of chromomycosis with tuberclelike formation. The verrucose phialophora organisms were abundant in the infected tissue.

In the second case the lesion was primary on the helix of the right ear and was of two months' duration. It was raised and ulcerative, and clinically resembled squamous-cell carcinoma. The etiological agent was not cultured but the histopathological picture was characteristic of chromomycosis. However, in this case, instead of the granulomatous tissue changes so marked in the first case, there was an infiltration of various types of cells, chiefly polymorphonuclear leucocytes with many fungous cells.

A detailed description is given of the etiological organism, the clinical features, the histopathological structure, and the prognosis and treatment of the lesion.

EDWARD W. GIBBS, M.D.

Herrell, W. E., and Heilman, D.: Tissue Culture Studies on Cytotoxicity of Bactericidal Agents. Cytotoxic and Antibacterial Activity of Gramicidin and Penicillin. Comparison with other Germicides. *Am. J. M. Sc.*, 1943, 206: 221.

A comparison was made of the bactericidal and cytotoxic activity of gramicidin, penicillin, merthiolate, zephiran, phemerol and sodium sulfathiazole against one strain each of diplococcus pneumoniae, staphylococcus aureus, and streptococcus pyogenes. Bits of tissue from the mesenteric lymph node of the rabbit in a medium consisting of a drop of heparinized rabbit's plasma and 3 drops of an extract of chick embryo in rabbit's serum was used for the toxicity tests. For the bactericidal tests a suitable dilution of broth culture of the organism tested was added to this same tissue extract so as to allow the growth of 20 or more colonies in each tissue culture preparation. The least amount of germicide that would completely prevent the appearance of bacterial colonies in all cultures (4 duplicates were made for each experimental condition) after incubation at 37°C. for forty-eight hours was determined for each bacterial strain.

Results showed the order of decreasing toxicity to be merthiolate, zephiran, phemerol, gramicidin, sodium sulfathiazole, and penicillin by this test. Penicillin was very effective against all three bacterial strains. Small amounts of gramicidin prevented the growth of pneumococci and hemolytic streptococci, but large amounts were necessary to prevent the growth of staphylococci. The germicides were effective against the test organisms, but sodium sulfathiazole was ineffective unless concentrations in excess of 0/1 per cent were used. Penicillin was superior to the other germicides tested because it was least toxic of all the test substances. Gramicidin was less toxic than the other germicides, but comparable in toxicity to the two detergents zephiran and phemerol. The catonic detergents, furthermore, are hemolytic in small concentrations in the presence of serum.

The antibacterial activity of gramicidin, which behaves like an anionic detergent, can be neutralized by the cationic detergent, phemerol. The simultaneous use of gramicidin and a cationic detergent in the treatment of infections is contraindicated. There is no contraindication to the simultaneous use of gramicidin with penicillin or anionic detergents including ordinary soaps. EDWIN J. PULASKI, M.D.

SURGICAL PATHOLOGY AND DIAGNOSIS

Stout, A. P.: A Discussion of the Pathology and Histogenesis of Ewing's Tumor of Bone Marrow. *Am. J. Roentg.*, 1943, 50: 334.

Ewing's tumors of the bone marrow are rare. From 1906 to the present only 42 cases have been available for study. These emanated from Columbia University and other sources.

Fourteen of the 42 cases were treated by radical resection. Autopsies were obtained and studied in 2. The histopathological studies were meager. This was due primarily to the lack of available material and, secondly, to the ruined specimens caused by radiation necrosis.

Analysis and study of the author's series, together with those of other writers, revealed Ewing's tumors to be more common in the male (60 per cent). They were found, in general, during early childhood and youth; however, the age of the patients varied from four to seventy-nine years. Tumor growth was rapid, the symptoms generally having been present for less than one year; pain occurred in 80 per cent of the cases. In some instances fever and leucocytosis also were present. Although the tumor started in the bone, it spread by extension to the adjacent tissue in all of the cases.

Originating anywhere in the soft part of the bone, the tumor was rarely found in the epiphysis. It formed neither bone nor cartilage. Grossly, the tumor tended to be soft and had a pallid color, probably because of necrosis and hemorrhage. Tumor infiltrated inside and outside of the bone. Metastasis occurred by hematogenous routes and was commonly seen in the lungs and bones.

Histologically, the tumor consisted of solid cords of cells separated by bands of fibrous tissue. The size of the cell varied, usually from two to four times that of a lymphocyte, and the shape was round. Pseudorosettes were made up of columnar epithelium, arranged in a ball with the nuclei in the periphery and the cytoplasm toward the center. Other authors have reported the presence of an embryonal type of red blood cell, myelocytes, plasma cells, and macrophages.

The histogenesis of Ewing's tumor is unknown. Ewing believes the tumor originates from the vascular endothelium with angioblastic properties. Oberling believes it is a reticulosarcoma with young reticular cells. The author is of the opinion that before the histogenesis of tumors can be settled, more experimental studies will have to be done.

MAURICE D. SACHS, M.D.

EXPERIMENTAL SURGERY

Nedzel, A. J.: Experimental Production of Gastric Ulcers in Dogs by the Induction of Vascular Spasm with Pitressin. *Am. J. Digest. Dis.*, 1943, 10: 283.

Clinical, experimental, and post-mortem observations on the pathogenesis of gastric or duodenal ulcers furnish many conflicting views.

Virchow proposed the theory that ulcers are caused primarily by nutritional disorders of the vessels, resulting from thrombi and emboli, which by interfering with the circulation lead to hemorrhagic infarct and to necrosis.

Von Bergmann founded a spasmogenic theory of ulcer development. According to him the disturbances in the sympathetic nervous system are factors that in many cases cause the spastic vascular contraction, and circumscribed anemic regions are developed which are attacked by the digestive fluids. Loss of peptic substance may evoke new spasms that will interfere with the healing process.

Rossle offered a conception of ulcer as a secondary disease, the result of a neuroreflex action.

Stewart believed that the most frequent mechanism causing ulcer appears to be a focus of necrosis from vascular obstruction or stasis, a condition which can be brought about by a spasm of the arteries or of the stomach itself.

Hurst emphasizes the importance of hyperasthenic, duodenal, and gastric diathesis in ulcer.

Palier considers the local cause of ulcer formation as a chemicomechanical one, and the underlying cause a constitutional one, namely, a disturbance of metabolism.

Carlson and Rivers pointed out that the factor common to all peptic ulcers is the fact that the lesions occur only in tissues bathed by the acid-pepsin gastric chyme.

Abrumyantz and Zabusova concluded that prolonged fasting intervals and irregular eating caused by certain occupations play an important part in the pathogenesis of gastrointestinal ulcerations.

Smithies points out that the productive gastric or duodenal ulcer evidently consists in disturbances of the normal arterial blood circulation in the gastrointestinal wall.

Robinson advances the psychogenic theory. He states that this disease is found among the susceptible individuals of the long thin type who are given to worry and nervous instability.

Von Bergmann and others stress the view that gastric ulcer is a manifestation of a systemic disease and should not be considered as a local disorder.

Callahan and Ingham conclude from their clinical observations that there seems to be a correlation between peptic ulcer and body build, personality, and other characteristics.

Ask-Upmark presents evidence to support the opinion that a definite relationship exists between the liver, carbohydrate metabolism, and the central nervous system.

Practically all the many ingenious methods of producing peptic ulcers experimentally involve the integrity of the local blood supply, and lead in one way or another to nutritional changes in the walls of the stomach or the duodenum.

Shapiro and Ivy established the anaphylactic nature of the local gastric reaction obtained by the employment of egg albumin, beef protein, oat protein, squash seed, globulin, edestin, hemoglobin, and horse serum.

Friedenwald, Feldman, and Morrison produced ulcers in most instances by the injection of a 1 per cent hydrochloric acid solution into the gastric tissue.

Hanke injected caffeine in cats with an empty stomach.

Westphal and Kuckuck experimented on dogs, which under anesthesia received faradic current on the vagus nerve and injections of suprarenin.

Dodds and his coworkers, and Nedzel show that pathological lesions may be produced in the gastrointestinal tract of animals by injecting extracts of the posterior lobe of the pituitary gland.

Windwer and Matzner produced experimental gastric ulcers in rats by their pepsin-hydrochloric-acid method.

There is one thing in common in the clinical, pathological, and experimental observations upon which the various views on the etiology and pathogenesis of gastric and duodenal ulcers are based—any interference or disarrangement of the normal nutrition function of the gastroduodenal walls may lead to pathological changes in the corresponding regions and ultimately to ulcer formation.

All the experiments in this study were made on 62 dogs by administering a single injection or repeated injections of pitressin intravenously. Two injections weekly were given until a total of 50 injections was reached. Thirty-nine dogs gave negative and 23 positive results. The latter showed lesions of the stomach and duodenum ranging from a small erosion to a large ulcer.

Direct observation was made by exposing the stomach in its front wall near the pylorus, and at different stages of the observed changes specimens of tissue were taken from the stomach, which were stained and studied histologically.

The direct observations and histological findings point to a condition of the blood vessels as the immediate cause of ulcer formation, and indicate that the "spasm theory" is the most logical one to explain the periodicity, appearance, and distribution of ulcers in the stomach and duodenum.

Pitressin injected intravenously evokes spasms of the small blood vessels and muscular tissues. The contraction is followed by dilatation, and if contraction is prolonged or exaggerated, the parenchymal cells will become injured, because of an undue general or local anoxia.

An explanatory note by the editor reveals that this article forms a part of a series of experiments related to the effects of pitressin-induced vascular spasm in dogs, and is taken from a monograph written by the author on the subject of vascular spasm, in which the production of lesions of such diverse diseases as endocarditis, multiple sclerosis, and gastric ulcers are discussed. It is considered that the pathological findings deserve careful consideration by all gastroenterologists in spite of the general iconoclastic character of the theme.

STEPHEN A. ZIEMAN, M.D.

Dunn, J. S., and McLetchie, N. G. B.: Experimental Alloxan Diabetes in the Rat. *Lancet*, Lond., 1943, 245: 384.

Dunn, McLetchie, and Sheehan had previously produced acute selective necrosis of the pancreatic islets in rabbits with pure chemicals, particularly alloxan.

In the present study with rats, alloxan was injected subcutaneously or intramuscularly, in doses of from 300 to 400 mgm. per kgm. of body weight, which usually caused severe acute damage of the islets of Langerhans. In some cases there was also necrosis in the renal tubules. Glycosuria developed in 5 rats which survived a series of injections. Two of the rats exhibited almost all of the symptoms and signs of severe diabetes mellitus, while a third rat, with symptoms of moderate severity, appeared to be recovering after two months. The glycosuria could be abolished by injections of insulin. Pathological changes of varying severity, extreme in 2 cases, were found in the pancreatic islets in these diabetic rats. WALTER H. NADLER, M.D.

Fine, J., and Seligman, A. M.: Traumatic Shock. *Ann. Surg.*, 1943, 118: 238.

Traumatic shock is a state of vascular collapse in which these phenomena are observed: (1) the cardiac output is greatly diminished; (2) the velocity of flow through the peripheral vascular bed is reduced; (3) acid metabolites are present in increased concentration in the blood; (4) the blood carbon-dioxide concentration is usually diminished; (5) venous oxygen concentration is much reduced, while arterial oxygen concentration may be normal or slightly reduced; (6) the volume of venous return to the heart is reduced; and (7) the blood pressure eventually falls.

The focal point of the functional disturbance is in the peripheral vascular bed. Consequently, urine excretion is diminished, the oxygen consumption is lowered, and the body surface is ischemic. Plasma volume depletion explains some but not all of the phenomena of shock, and plasma replacement will restore the organism, but not if the shock has persisted for some time. The popular explanation for this failure is that the replaced fluid fails to remain in the blood stream because of damage to the capillary walls. Direct evidence for the existence of capillary damage outside of the area of injury is not conclusive.

The authors employed plasma proteins containing synthesized radioactive sulfur, bromine, and iodine for the determination of the degree to which capillary

permeability is altered in traumatic shock. Hemorrhagic, burn, and tourniquet shock were studied. No evidence of leakage due to change in the permeability of the general capillary bed was found, which contradicted the theory that such damage results in widespread extravascular loss of plasma. Except in burn and tourniquet shock a local loss of plasma as such is usually insignificant. While plasma loss is the most significant initiating cause of shock, the irreversibility of the shock state is not due to a progressive decline in plasma volume, but rather to a progressive deterioration of the peripheral circulatory mechanism, characterized by decreased volume flow and velocity of the flow through the capillaries. The most important factor is the stagnation or trapping of about one-fifth of the capillary blood out of the circulation as the shock phase deepens. The blood content in cubic centimeters per gram of tissue is not more, but generally the same, or less, in dogs presenting shock than in normal dogs.

The therapeutic problem in shock after adequate replacement of blood or plasma has failed is one of restoring the volume and the velocity of the flow through the capillaries before the integrity of vital tissue processes is inevitably lost. Various substances which may improve the peripheral circulation in shock are being investigated. It has been found that pressor amines and pure oxygen do not produce such improvement.

EDWIN J. PULASKI, M.D.

Phemister, D. B.: Role of the Nervous System in Shock. *Ann. Surg.*, 1943, 118: 256.

The great objection to the neurogenic theory of shock is the lack of evidence based on carefully controlled clinical and experimental studies in which other factors, such as local loss of circulating fluid and anesthesia, are excluded. The most popular conception of neurogenic shock is that it results from marked and prolonged lowering of the blood pressure by afferent vasodepressor impulses coming to the vasomotor center over somatic nerves, or from the cerebral cortex, as in syncope. Lowering of the blood pressure is accomplished by the inhibition of vasoconstrictor impulses and possibly by acceleration of the vasodilator impulses. Cardiac inhibition is also a causative factor in syncope. Experimental alternating stimulation of the somatic nerves for from one to two hours with a tetanizing current may produce a fall in pressure to some extent, but produces nothing like a state of shock. The marked lowering of the blood pressure in fainting is quickly overcome with the loss of consciousness, the interruption of adverse psychic impulses, and the recumbent position.

In this study the cardioaortic or aortic depressor nerves in rabbits were stimulated, as were the carotid sinus nerves in dogs in a previous study. The animals were lightly anesthetized with urethane administered intraperitoneally. When the blood pressure was maintained at low levels by continuous cardioaortic nerve stimulation, death took place in from two and one-half to eight hours and, in general, the lower the pressure, the shorter the period of survival. Temporary interruption of the stimulus during the earlier periods of the experiment usually resulted in a rapid rise of pressure to the vicinity of the previous level, which indicated a good state of vasomotor tone. Later in the experiments interruption of the stimulus did not produce a favorable response, and this indicated failure of the vasomotor tone. Blood examination showed hemodilution and reduction of the arterial blood oxygen and carbon dioxide. In some cases there was a tendency toward hemoconcentration toward the termination of the survival period. When the vasomotor tone was well preserved, permanent release of the stimulus would be followed by rapid restoration of the blood pressure to prestimulation levels and the animals lived on, similarly to the controls. The blood, which usually became diluted during the period of low blood pressure, would show a tendency to concentrate after the pressure was again elevated. This is evidence that the blood pressure may be maintained at shock levels for long periods by a purely nervous reflex vasodepressor mechanism, without serious impairment of either the vasomotor center or the peripheral circulation, and that the circulation may rapidly return to normal after the stimulation is stopped.

When the blood became considerably diluted and vasomotor tone showed signs of failure following a prolonged period of low pressure, the transfusion of either whole blood or plasma brought about a period of definite improvement in the circulation. Although the level of the blood pressure during stimulation was elevated little, the survival period was prolonged, the response on release of the stimulus was improved, and the bleeding volume of the animal compared favorably with that of the control animals.

The effect of neurogenic lowering of the blood pressure was also tested on animals already in a state of impending or actual shock as a result of hemorrhage. In these experiments vasodepression from nerve stimulation usually shortened the survival time. In other experiments the animals' tolerance to bleeding was tested after prolonged cardioaortic nerve stimulation. The bleeding volume showed only a slight-to-moderate reduction compared to that of the controls, which indicated that the circulation was, on the whole, remarkably well preserved. Determinations of the circulating blood volume during vasodepression showed reduction in total volume, plasma volume, and red cell mass.

Further evidence that the blood pressure may be reduced to low shock levels for prolonged periods by a neurogenic mechanism before circulatory failure occurs was obtained by sectioning of the seventh cervical segment of the spinal cord in dogs. This procedure resulted in severe and prolonged lowering of the blood pressure before failure of circulation occurred.

Results such as were obtained in this study have never been produced by direct stimulation of the somatic nerves. It is highly improbable in the case of accidental or operative wounds that shock ever re-

sults from the action of afferent vasodepressor impulses traveling over the injured somatic nerves primarily. Neurogenic shock can be produced experimentally by prolonged electrical stimulation of the cardioaortic or aortic depressor nerves in the rabbit, but neurogenic factors are probably never the primary cause of traumatic or surgical shock. When combined with hemorrhage, neurogenic factors may contribute to the development of shock. Blood and plasma loss and the toxicity of anesthetics are relatively of far greater importance in shock production than neurogenic factors. JOHN L. LINDQUIST, M.D.

Parkins, W. M., Koop, C. E., Riegel, D., Vars, H. M., and Lockwood, J. S.: Gelatin as a Plasma Substitute, with Particular Reference to Experimental Hemorrhage and Burn Shock. *Ann. Surg.*, 1943, 118: 193.

Normal dogs tolerate repeated infusions of large volumes of gelatin-saline solution without any serious toxic reaction specific to gelatin. However, any unfavorable reactions that occur are reversible, and are frequently produced by infusions of comparable amounts of saline solution or plasma.

Pseudoagglutination of erythrocytes and increase in sedimentation rate, which occur also after the infusion of other macromolecular colloids, have been observed in vitro and in vivo after gelatin infusions.

Bromsulfalein retention occurred after repeated infusions of gelatin, but is present to some extent also in dogs infused with comparable volumes of plasma. Other liver-function tests were essentially negative. Kidney function, as determined by urea clearance, was apparently unimpaired after repeated infusions of gelatin in normal dogs.

Tissue changes observed histologically were reversible and slightly more marked with gelatin than with plasma, infused in equal volumes and under similar conditions. No chronic tissue storage was observed in animals which received repeated infusions of large volumes of gelatin.

A transient diuresis and excretion of gelatin followed the infusion of gelatin in normal dogs and in dogs subjected to preliminary hemorrhage. About half of the gelatin was excreted in the urine.

Following massive, rapid hemorrhage and immediate infusion of gelatin, the plasma proteins were apparently replaced at about the same rate as that at which gelatin protein disappeared from the blood stream. All dogs survived a rapid massive hemorrhage to the point of respiratory failure and blood pressure levels of about 20 mm. of mercury if they were immediately infused with either saline solution or gelatin. The higher total protein concentration following gelatin infusion, the considerably greater hemodilution, and the more rapid return of the blood pressure to normal strongly bear out the superiority of gelatin over saline solution in experimental hemorrhage of this type. The resistance of the dogs to repeated massive hemorrhage followed by gelatin infusion is markedly increased over that of the animal similarly bled and infused with saline solution. The saline-infused dog in which the blood pressure continued to decline and remained at critical levels for hours after repeated infusions completely recovered upon subsequent infusions of gelatin.

Following a slow hemorrhage with the blood pressure maintained at between 30 and 40 mm. of mercury for from thirty to forty minutes, all untreated dogs succumbed within a few hours. Although elevations of the plasma volume and of the blood pressure were not marked or well maintained after the infusion of saline solution, compensation occurred and 2 of 5 dogs slowly recovered. Three of the saline-treated animals died in from two to six hours. Gelatin infusion resulted in a more marked hemodilution than did plasma infusion under uniform volume replacement. The blood pressure was restored and maintained at approximately the same levels with gelatin as with plasma, and all dogs made a rapid, complete recovery. Under these conditions of experimental hemorrhage, gelatin appears to be a suitable substitute for plasma.

In 8 dogs, subjected to a standardized, reproducible burn of a degree fatal to untreated animals and to a majority of saline-infused animals, gelatin solutions compensated for the loss of plasma from the blood stream, and corrected hemoconcentration to the same degree as did plasma infusion in 4 animals. Although survival was extended in the group receiving gelatin for shock from burns beyond the period when death occurred in the controls, presumably from hemoconcentration, 7 of 8 dogs succumbed after progressive decline in the blood pressure, unassociated with hemoconcentration. Under identical conditions with plasma infusion, only 1 of 4 dogs succumbed.

If a factor can be identified in plasma which accounts for its ability to maintain blood pressure in the severely burned animal during the secondary phase of so-called acute toxemia, the addition of this factor to gelatin may result in a better plasma substitute for burns. SAMUEL KAHN, M.D.

Elman, R., and Lischer, C. E.: Amino-Acids, Serum, and Plasma in the Replacement Therapy of Fatal Shock Due to Repeated Hemorrhage. *Ann. Surg.*, 1943, 118: 225.

Fatal surgical shock was produced experimentally by rapid bleeding (10 cc. per kgm. every hour) of unanesthetized dogs. Death occurred after an average of 40 cc. of blood per kgm. had been removed, and the mean survival time was three and six-tenths hours. The amount of blood removed in a single bleeding was less often fatal. Accompanying the repeated bleedings was a progressive fall in the blood pressure, in the red-cell volume, and in the plasma albumin and globulin.

Immediate replacement of the volume of lost blood by a solution of 10 per cent glucose in normal saline solution did not alter the survival time. However, if a 5 per cent glucose solution contained 5 per cent of the amino acids of hydrolyzed casein or beef serum, the survival time was increased from three and six-

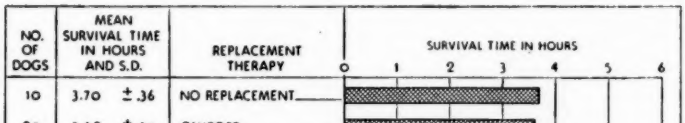
NO. OF DOGS
MEAN SURVIVAL TIME IN HOURS AND S.D.
REPLACEMENT THERAPY
SURVIVAL TIME IN HOURS
0 1 2 3 4 5 6
10 3.70 ±.36 NO REPLACEMENT
20 3.62 ±.31 GLUCOSE
6 4.25 ±.37 PURE AMINO ACIDS
10 4.50 ±.36 SERUM
10 4.60 ±.38 CITRATED PLASMA
20 5.15 ±.23 PROTEIN HYDROLYSATE
10 6.00 ±.23 HEPARINIZED PLASMA

Fig. 1. Survival-times in the 7 groups of experiments described in the text: S.D.-standard deviation, calculated according to usual statistical formulas. Note that replacement with heparinized plasma and a protein hydrolysate gave the longest survival time, and the relatively poor showing with serum and citrated plasma. (Courtesy of J. B. Lippincott Co.)

tenths hours to five and one-tenth hours. A comparative study of the effect of immediate replacement with pure amino-acid solutions, serum, citrated plasma, and heparinized plasma showed the first three were no better than the protein hydrolysate. The heparinized plasma was the best of all, the survival time being increased to six hours. The fall in blood pressure was greater with citrated plasma and serum than with heparinized plasma, whereas hydrolyzed protein produced less hypotension than glucose solution.

A study of the changes in the red-cell volume and in plasma protein gives some indication that the amino acids of hydrolyzed protein were converted into plasma albumin. Microscopic observations of biopsy specimens of the liver indicated that protein is lost from the hepatic cytoplasm in hemorrhage, and that injecting hydrolyzed protein replenishes this loss, and thus enables the animal to withstand further loss of blood more effectively.

The administration of amino acids thus provides a simple and direct means of correction of tissue-protein depletion and of the concomitant negative nitrogen balance attending traumatic shock. If whole blood or plasma is not available, it would seem that protein hydrolysate is preferable to crystalloid in the treatment of shock due to hemorrhage.

In the discussion, evidence was presented that too much of the citrate used in citrated plasma has a toxic and deleterious effect, particularly by virtue of the resulting increased coagulability of the blood; this explains the superior results obtained from heparinized plasma. EDWIN J. PULASKI, M.D.

Muirhead, E. E., Ashworth, C. T., Kregel, L. A., and Hill, J. M.: The Therapy of Shock in Experimental Animals with Serum Protein Solutions. Fate in the Body of Concentrated and Dilute Serum and Saline Solutions. *Surgery*, 1943, 14: 171.

In this study the authors have observed the fate in the body of intravenously administered concentrated serum, dilute or half-strength serum, and 5 per cent glucose in physiological saline solution. As experimental animals they used dogs in which one hind limb had been severely frozen to produce a marked decrease in plasma volume and a fatal shock. This type of shock is similar to wound or traumatic shock and other types of shock without a large loss of blood.

The essential changes observed are a loss of plasma fluid, hemoconcentration, hypotension, decrease in total circulating proteins, acidosis, decrease in the thiocyanate available fluid, plasma sodium concentration, hemoglobinemia, capillarovenous stasis, i.e., packing in the capillaries of great numbers of red cells, and other visceral changes. When a severe hypotension occurred, the re-establishment of the plasma volume improved the circulation temporarily but did not save the life of the animal.

Concentrated serum produced an increase in plasma volume greater than the volume given, which indicated a shift of fluids into the plasma stream probably from the tissue. The shift of fluids constituted a directional flow opposite to that occurring in the pathogenesis of shock and a reversal of the abnormal mechanisms occurring in the capillaries. The effects produced by the injection of concentrated serum were in direct proportion to the volume given.

Dilute serum in large volumes improved the circulation but at the same time fluid escaped from the vascular system in substantial volumes, further protein was lost, and capillarovenous stasis was not substantially improved.

Glucose-saline solution was rapidly lost from the circulation and the ultimate effects were deleterious since further protein was lost and the circulatory insufficiency became more pronounced.

The comparison of dilute serum and concentrated serum on the basis of the total amount of protein administered revealed a superiority of concentrated serum over dilute serum in coping with the circulatory abnormalities. CONRAD L. PIRANI, M.D.

Elman, R., Charnas, R., and Davey, H. W.: The Ceiling of Utilization of Nitrogen: Effect of Continuous Venoclysis with the Amino Acids of Hydrolyzed Protein during Experimental Hypoalbuminemia. *Arch. Surg.*, 1943, 47: 216.

The correction of protein deficiencies of nutritional origin is a serious quantitative problem whenever the depletion is so severe as to require a large amount of protein alimentation. If but a short time is available for correction, the difficulties are multiplied. Moreover, in many cases the parenteral route must be used. The purpose of the study reported here was to determine if possible the ceiling of utilization of intravenously given amino acids and polypeptides, i.e., how rapidly protein depletions can be corrected. An analogy may be drawn between this problem and that of vitamin deficiencies, many of which may often be corrected completely within a few hours or days by giving sufficiently large doses of vitamins.

As far as could be determined, no previous observations have been made with intravenous injections of really large doses of mixtures of amino acids. In the St. Louis City Hospital as much as 300 gm. of hydrolyzed casein daily for three days has been so administered to 2 patients without difficulty. In a study by Brunschwig, Clark, and Corbin the greatest amount of the same hydrolysate injected in one day was 150 gm. for ten consecutive days for a patient weighing 50 kgm.

Positive nitrogen balance as well as regeneration of serum albumin was demonstrated in protein-depleted dogs when 1.75 gm. of nitrogen per kilogram per day was given for two days by means of a continuous venoclysis, an enzymic hydrolysate of casein containing a mixture of amino acids and polypeptides being used as the sole source of nitrogen. When this same total dose of nitrogen was given during twenty-four hours there was evidence of much less complete utilization. On the basis of the evidence presented, it would seem that the body has a much greater capacity for utilizing intravenously administered amino acids and polypeptides than is generally supposed. J. M. MORA, M.D.

Hubbard, R. S., and Porter, R. C.: The Glycolytic Enzymes of Synovial Fluid. *J. Lab. Clin. M.*, 1943, 28: 1328.

In 1936 the authors reported certain actions of glycolytic enzymes in cerebrospinal fluid from patients with epidemic meningitis. Evidence was presented showing that while the larger part of the reducing sugar (glucose) in such spinal fluid disappears quite rapidly on incubation, the trace of fructose which is present is destroyed very slowly. Other experiments showed that the enzyme which catalyzed the reaction was present in the cellular elements, and indirect evidence was presented which tended to prove that the enzyme was present in the polymorphonuclear leucocytes of the fluid.

Recently the authors had an opportunity to study the glycolytic enzymes of synovial fluid. A patient with a sterile inflammatory reaction of the knee joint supplied the synovial fluid, which on aspiration was found to be free from organisms but very rich in polymorphonuclear leucocytes. The authors report the results of experiments upon the destruction of both glucose and fructose when added to this synovial fluid.

Repeated careful examinations of this synovial fluid led the authors to believe that it was completely sterile. In carrying out the experimental procedures 6 different samples of synovial fluid were used. The cell contents of these fluids varied markedly, but all were very high. In some studies the cells were first removed by centrifuging, and in others untreated fluids were used. These fluids were divided into portions of approximately 6 cc. In many instances small amounts, usually 0.6 cc. of concentrated sterile solutions of the purest glucose or fructose obtainable were added to these 6 cc. portions; and then sterile water was added in an amount equal to the volume of each of the mixtures. These treated solutions were then mixed as thoroughly as possible in an attempt to prepare equal concentrations of cellular elements, and divided into three equal parts, each of which contained approximately 2 cc. One of these was analyzed at once; one was placed in an incubator at 37° C.; and one was placed in the ice box.

There were 6 different sets of experiments, all of which gave significant results. These are carefully tabulated by the authors.

The important observation brought out by these experiments was that when glucose or fructose was added to sterile synovial fluid which was rich in polymorphonuclear leucocytes, the sugars were destroyed. The rate of the destruction of glucose was at least twice as great as was that of fructose. The enzymes were present almost wholly in the cells, although they could occasionally be demonstrated in the cell-free fluid. Qualitatively the results confirm those previously obtained with cerebrospinal fluid.

MATHIAS J. SEIFERT, M.D.

Baker, R. D., and Handler, P.: Animal Experiments with Tannic Acid. *Ann. Surg.*, 1943, 118: 417.

Since about 1925 tannic acid has been widely used in this country and abroad in the treatment of cutaneous burns, by spraying on aqueous solutions, by bathing the patient in aqueous solutions, or by applying an ointment to the burned area. The most serious drawback to the use of tannic acid to date has been the charge that it is absorbed from the region of application and causes damage to the liver. Since 1938, at least four communications have appeared which describe impressive central necrosis of the liver in patients who have been burned and have had some form of tannic-acid therapy, whereas articles on fatal burns which appeared before the use of tannic acid do not emphasize hepatic necrosis as characteristic of burns.

Evidence has begun to accumulate that tannic acid damages the livers of animals when it is absorbed from a burned area or from the subcutaneous

tissues. Dogs burned experimentally and then treated with tannic-acid ointment showed hepatic necrosis, but, since no control experiments were performed in which tannic acid was applied in the absence of the burn, the comparative role of the burn and the tannic acid in the production of hepatic necrosis is difficult to evaluate. Following subcutaneous injections of tannic acid (U. S. P.) into white rats, severe hepatic damage has been observed. These lesions consisted of central necrosis comparable to that noted in autopsies of burned patients who had been treated with tannic acid; and the degree of liver damage in the rats was in direct proportion to the amount of tannic acid injected subcutaneously.

In the experiments it was desired to amplify those already made on rats, and to determine the importance of the various factors involved, in order to judge the applicability of tannic acid to the treatment of human burns, insofar as the experimental results might aid in the settling of this problem. Four series of animal experiments were undertaken.

Experiments verifying the observation that subcutaneous injections of tannic acid produce hepatic necrosis were made on rats and white mice. Neutralized tannic acid of *p*H. 7.2 injected subcutaneously was as damaging to the liver as the tannic acid (U. S. P.) of *p*H. 3. Gallic acid introduced subcutaneously produced no hepatic damage, which indicated that it is not the gallic acid component of tannic acid which is responsible for the necrosis of the liver.

Experiments to determine whether tannic acid is absorbed when applied to a body surface denuded of skin, revealed hepatic necrosis was produced in rats by removing the ventral skin, immersing the rat in a tannic acid bath for a period of fifteen minutes, and washing the treated area with tannic acid the following day. Minor hepatic necrosis occurred in some of the rats when one-fourth of the skin of the body was removed and solutions as low as 2.5 per cent were applied. Severe hepatic necrosis was produced by 20 per cent tannic acid applied to an area of the same size, and some of the rats which received this concentration died. In control experiments in which other rats were treated with water in the same manner, no hepatic necrosis was noted. Tannic acid produced hepatic necrosis whether aqueous solutions or ointments were used. Tannic acid of 10 per cent concentration, or less, sometimes produced necrosis of viable tissue over the denuded areas, and this occurred regularly when concentrations greater than 10 per cent were employed.

Experiments to determine whether tannic acid or some derivative thereof can be excreted in the urine, after the subcutaneous injection of tannic acid, revealed a substance in the urine which turned black on the addition of ferric chloride.

Experiments to determine whether tannic acid (U. S. P.) can be purified further, so as to avoid hepatic damage, revealed that the purified tannic acid had the same action in the experimental animal as the tannic acid (U. S. P.).

Direct application of these experimental results to the treatment of human burns with tannic acid should be made with extreme caution, especially when dealing with absorption from a skinned area, since absorption from burns has not been investigated in this study. JOHN E. KIRKPATRICK, M.D.